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=> fil hcap
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FILE COVERS 1907 - 28 Dec 2007  VOL 148 ISS 1
FILE LAST UPDATED: 27 Dec 2007  (20071227/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que l38
L5                STR
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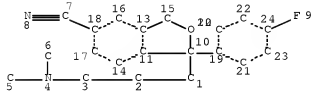

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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS  24

STEREO ATTRIBUTES: NONE
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L7            29 SEA FILE=CAPLUS ABB=ON  PLU=ON  L6(L)PUR+NT/RL
L9           143 SEA FILE=CAPLUS ABB=ON  PLU=ON  L6(L)PREP+NT/RL
L10           22 SEA FILE=CAPLUS ABB=ON  PLU=ON  L6(L)(PURIF? OR RECOVER?)
L11           42 SEA FILE=CAPLUS ABB=ON  PLU=ON  L7 OR L10
L12           15 SEA FILE=CAPLUS ABB=ON  PLU=ON  L6(L)PURIF?
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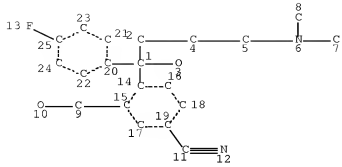

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE
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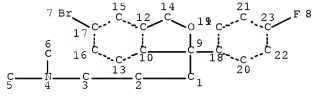
L19 STR



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

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L24	12	SEA FILE=CAPLUS ABB=ON PLU=ON L23 AND L11
L25	35	SEA FILE=CAPLUS ABB=ON PLU=ON L24 OR L13
L26	1762	SEA FILE=CAPLUS ABB=ON PLU=ON L6(L)(BAC OR DMA OR PAC OR PKT OR THU)/RL
L29	2478	SEA FILE=HCAPLUS ABB=ON PLU=ON "5-HT REUPTAKE INHIBITORS"+PFT/CT
L30	533	SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND L26
L31	3	SEA FILE=HCAPLUS ABB=ON PLU=ON L30 AND L11
L32	37	SEA FILE=HCAPLUS ABB=ON PLU=ON L31 OR L25
L33	2	SEA ("UTTARWAR S G"/AU OR "UTTARWAR SUNIL GOVINDRAO"/AU)
L34	2	SEA ("GAWLI B N"/AU OR "GAWLI BHAGWAN NARAYAN"/AU)

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L35            2 SEA (L33 OR L34)
L36            1 DUP REM L35 (1 DUPLICATE REMOVED)
L37            1 SEA FILE=HCAPLUS L36
L38           37 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32 OR L37


=> d l38 ibib abs hitind hitstr tot

L38  ANSWER 1 OF 37  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:1128470  HCAPLUS  Full-text
DOCUMENT NUMBER:          147:528009
TITLE:                    New process for the preparation of high pure
                          citalopram salts
INVENTOR(S):              Satyanarayana, Chava; Haribabu, Bodepudi;
                          Ramanjaneyulu, Gorantla Seeta; Jyothibasu, Abbineni;
                          Rao, Chunchu Venkata Ramana
PATENT ASSIGNEE(S):       Matrix Laboratories Ltd., India
SOURCE:                   Indian Pat. Appl., 16pp.
                          CODEN: INXXBQ
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     --------------      ----   --------    -------------------    --------
     IN 2003MA00329       A     20070706    IN 2003-MA329          20030421
PRIORITY APPLN. INFO.:                      IN 2003-MA329          20030421
AB   The present invention claims the usage of excess cuprous cyanide to get the 5-
     bromo analog levels to less than 0.3% in the crude citalopram, and rapid
     process for the isolation of pure citalopram salts in the absence of or with
     low levels ( <0.1 %) of the impurities by the judicious selection of solvents
     and the manipulation of pH without employing elaborate workup procedures
     including crystallization techniques or expensive film distillation
IC   ICM  A61K031-343
CC   63-5 (Pharmaceuticals)
IT   59729-33-8P, Citalopram
     RL: PUR (Purification or recovery); SPN (Synthetic preparation);
     THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (new process for preparation of high pure citalopram salts)
IT   59729-33-8P, Citalopram
     RL: PUR (Purification or recovery); SPN (Synthetic preparation);
     THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (new process for preparation of high pure citalopram salts)
RN   59729-33-8  HCAPLUS
CN   5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-
     fluorophenyl)-1,3-dihydro-  (CA INDEX NAME)
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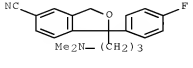
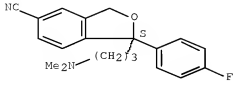


L38 ANSWER 2 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:691100 HCAPLUS Full-text
DOCUMENT NUMBER: 147:234934
TITLE: Substrate modification approach to achieve efficient resolution: didesmethylcitalopram: a key intermediate for escitalopram. [Erratum to document cited in CA146:316708]
AUTHOR(S): Elati, Chandrashekar R.; Kolla, Naveenkumar; Vankawala, Pravinchandra J.; Gangula, Srinivas; Chalamala, Subrahmanyeswarara; Sundaram, Venkatraman; Bhattacharya, Apurba; Vurimidi, Himabindu; Mathad, Vijayavitthal T.
CORPORATE SOURCE: Department of Research and Development, Dr. Reddy's Laboratories Ltd., Hyderabad, 502325, India
SOURCE: Organic Process Research & Development (2007), 11(4), 780
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB On page 292, in last paragraph, the correct exptl. details should read: "S-(=)-1-(3-Dimethylamino-propyl)-1-(4-fluoro-phenyl)-1,3-dihydro- isobenzofuran-5-carbonitrile (s-(+)-1•(-)-DPTTA). A mixture of compound 1a (25 g. 0.077 mol) and acetonitrile (125 mL) was stirred at room temperature for 5 min, and then a solution of (-) DPTTA monohydrate (31.4 g, 0.077 mol) in acetonitrile (125 mL) was added and the mixture stirred for 10-15 min. To the resultant white precipitate was added methanol (20 mL) slowly at 70-75°, and the resulting clear solution was slowly cooled to room temperature After cooling the flask to 0-5° for 1.0-1.5 h, the resulting solid was filtered. The recrystn. with acetonitrile/methanol was repeated for two more times, and the resulting solid was filtered. The filtered cake was washed with acetonitrile (20 mL) and dried at 60-65° to afford 9.8 g of 1·(-)-DPTTA. Yield (%): 36 (calculated relative to theor. which is half of the starting racemate). The DPTTA salt was hydrolyzed to afford escitalopram free base (1). [α]D for free base = 10.8 (c 1, methanol); chiral purity: 98.4%, H NMR for free base (200 MHz, DMSO-d6): 1.18-1.28 (m, 2H), 2.01 (s, 6H), 2.11-2.18 (m,4H), 5.11-5.20 (q,J=13.2 and 11.2 Hz, 2H), 7.12-7.16 (t, J + 8.8Hz, 2H), 7.56-7.59 (dd, j+5.2 and 3.6 Hz, 2H), 7.73-7.78 (m, 3H); MS (APCI) m/z 325 (M+ = 1).".
CC 27-6 (Heterocyclic Compounds (One Hetero Atom))
IT 928652-44-2P 928652-45-3P 928652-47-5P 928652-49-7P 928652-54-4P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(resolution of didesmethylcitalopram and further methylation to enantiopure escitalopram (Erratum))
IT 928652-44-2P 928652-47-5P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(resolution of didesmethylcitalopram and further methylation to enantiopure escitalopram (Erratum))
RN 928652-44-2 HCAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with (1S)-1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile (1:1) (CA INDEX NAME)

CM 1

CRN 128196-01-0
CMF C20 H21 F N2 O

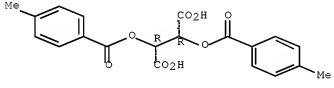
Absolute stereochemistry. Rotation (+).



CM 2

CRN 32634-66-5
CMF C20 H18 O8

Absolute stereochemistry. Rotation (-).

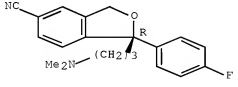


RN 928652-47-5 HCAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2S,3S)-, compd. with (1R)-1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile (1:1) (CA INDEX NAME)

CM 1

CRN 128196-02-1
CMF C20 H21 F N2 O

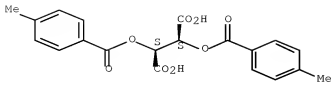
Absolute stereochemistry. Rotation (-).



CM 2

CRN 32634-68-7
CMF C20 H18 O8

Absolute stereochemistry. Rotation (+).



L38 ANSWER 3 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:91101 HCAPLUS Full-text
DOCUMENT NUMBER: 146:169401
TITLE: orodispersible tablets comprising crystalline base of escitalopram
INVENTOR(S): Dancer, Robert; Petersen, Hans; Nielsen, Ole; Rock, Michael Harold; Eliasen, Helle; Liljegren, Ken
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: U.S. Pat. Appl. Publ., 16pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2007021499	A1	20070125	US 2006-425522		20060621
PRIORITY APPLN. INFO.:			US 2005-693214P	P	20050622

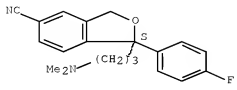
OTHER SOURCE(S): MARPAT 146:169401

AB The present invention relates to the crystalline base of the antidepressant, escitalopram, formulations of the base, a process for the preparation of purified salts of escitalopram, such as the oxalate, the salts obtained by the process and formulations containing such salts, and a process for the preparation of purified escitalopram free base or salts of escitalopram, such as the oxalate, using the hydrobromide, the salts obtained by the process and formulations containing such salts. Finally the present invention relates to an orodispersible tablet having a hardness of at least 22 N and an oral-disintegration time of <120 s and comprising an active pharmaceutical ingredient adsorbed onto a water soluble filler wherein the active pharmaceutical ingredient has a m.p. in the range of 40-100°, as well as a method for making such an orodispersible tablet. Thus, tablets contained fenofibrate 5.02, Peralitol SD200 136.46, Avicel PH102 25.02, AcDiSol 9.00, and Mg stearate 4.5 mg/tablet.

INCL 514469000; 549467000
CC 63-6 (Pharmaceuticals)
IT 128196-01-0P, Escitalopram
RL: PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(orodispersible tablets comprising crystalline base of escitalopram)
IT 128196-01-0P, Escitalopram
RL: PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(orodispersible tablets comprising crystalline base of escitalopram)
RN 128196-01-0 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L38 ANSWER 4 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:52599 HCAPLUS Full-text
DOCUMENT NUMBER: 146:316708
TITLE: Substrate Modification Approach to Achieve Efficient Resolution: Didesmethylcitalopram: A Key Intermediate for Escitalopram
AUTHOR(S): Elati, Chandrashekar R.; Kolla, Naveenkumar; Vankawala, Pravinchandra J.; Gangula, Srinivas; Chalamala, Subrahmanyeswarara; Sundaram, Venkatraman; Bhattacharya, Apurba; Vurimidi, Himabindu; Mathad, Vijayavitthal T.
CORPORATE SOURCE: Department of Research and Development, Dr. Reddy's Laboratories Ltd., Hyderabad, 502325, India
SOURCE: Organic Process Research & Development (2007), 11(2), 289-292
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
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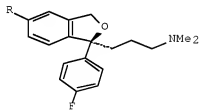

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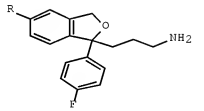


II

AB An approach to achieve the enantiopure escitalopram I (R = CN or Br) via didesmethyl escitalopram II, which is easily resolvable compared to citalopram I (R = CN) through diastereomeric salt crystallization was reported. The resolved intermediate (didesmethylcitalopram) was subsequently used for the preparation of the desired drug. This simple modification of the substrate makes a remarkable difference in the chemical resolution process. The first resolution of didesmethylcitalopram (±)-II to furnish (+)-II, a novel key intermediate to assemble escitalopram I (R = CN) was achieved via diastereomeric salt resolution using (-)-di-p-toluoyltartaric acid (DPTTA).

The resolution conditions were optimized; a key feature of this process is the addition of specific quantity of water at a specific temperature to the reaction mixture

CC 27-6 (Heterocyclic Compounds (One Hetero Atom))

IT 928652-44-2P 928652-45-3P 928652-47-5P 928652-49-7P
928652-54-4P
RL: PUR (Purification or recovery); SPN (Synthetic preparation);
PREP (Preparation)
(resolution of didesmethylcitalopram and further methylation to enantiopure escitalopram)

IT 928652-44-2P 928652-47-5P
RL: PUR (Purification or recovery); SPN (Synthetic preparation);
PREP (Preparation)
(resolution of didesmethylcitalopram and further methylation to enantiopure escitalopram)

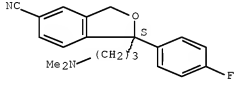
RN 928652-44-2 HCAPLUS

CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with (1S)-1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile (1:1) (CA INDEX NAME)

CM 1

CRN 128196-01-0
CMF C20 H21 F N2 O

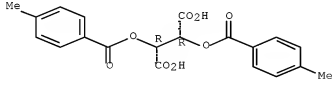
Absolute stereochemistry. Rotation (+).



CM 2

CRN 32634-66-5
CMF C20 H18 O8

Absolute stereochemistry. Rotation (-).



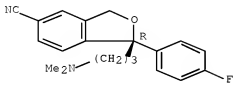
RN 928652-47-5 HCAPLUS

CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2S,3S)-, compd. with (1R)-1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile (1:1) (CA INDEX NAME)

CM 1

CRN 128196-02-1
CMF C20 H21 F N2 O

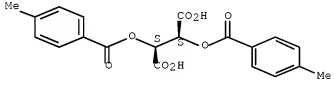
Absolute stereochemistry. Rotation (-).



CM 2

CRN 32634-68-7
CMF C20 H18 O8

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 5 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1357137 HCAPLUS Full-text
DOCUMENT NUMBER: 146:87640
TITLE: Orodispersible tablets comprising crystalline escitalopram
INVENTOR(S): Dancer, Robert; Petersen, Hans; Nielsen, Ole; Rock, Michael Harold; Eliasen, Helle; Liljegren, Ken
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 48pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006136169	A2	20061228	WO 2006-DK366	20060622
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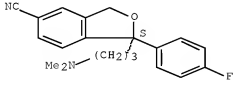
GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU,
SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG,
US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: DK 2005-912 A 20050622
OTHER SOURCE(S): MARPAT 146:87640

AB The present invention relates to the crystalline base of the antidepressant drug, escitalopram, formulations of the base, a process for the preparation of purified salts of escitalopram, such as the oxalate and a process for the preparation of purified escitalopram free base or salts of escitalopram, such as the oxalate, using the hydrobromide, the salts obtained by the process and formulations containing such salts. Finally the present invention relates to an orodispersible tablet having a hardness of at least 22 N and an oral-disintegration time of <120 s and comprising an active pharmaceutical ingredient adsorbed onto a water soluble filler wherein the active pharmaceutical ingredient has a m.p. in the range 40-100°, as well as a method for making such an orodispersible tablet.

IC ICM A61K
CC 63-6 (Pharmaceuticals)
IT 128196-01-0P, Escitalopram
RL: FMU (Formation, unclassified); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); USES (Uses)
(orodispersible tablets comprising crystalline escitalopram)
IT 219961-08-2P, Escitalopram oxalate 481047-50-1P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(orodispersible tablets comprising crystalline escitalopram)
IT 128196-01-0P, Escitalopram
RL: FMU (Formation, unclassified); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); USES (Uses)
(orodispersible tablets comprising crystalline escitalopram)
RN 128196-01-0 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



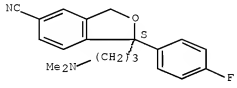
IT 219961-08-2P, Escitalopram oxalate 481047-50-1P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(orodispersible tablets comprising crystalline escitalopram)

RN 219861-08-2 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1), (1S)- (CA INDEX NAME)

CM 1

CRN 128196-01-0
CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (+).

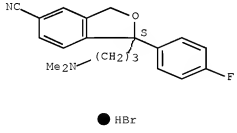


CM 2

CRN 144-62-7
CMF C2 H2 O4

RN 481047-50-1 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1), (1S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L38 ANSWER 6 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1356784 HCAPLUS Full-text
DOCUMENT NUMBER: 146:80528
TITLE: Chemoenzymatic process for the synthesis of escitalopram
INVENTOR(S): Cotticelli, Giovanni; Salvetti, Raul; Bertoni, Chiara

PATENT ASSIGNEE(S): Adorkem Technology SpA, Italy
SOURCE: PCT Int. Appl., 21pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006136521	A1	20061228	WO 2006-EP63193	20060614
WO 2006136521	A8	20070308		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

EP 1736550	A1	20061227	EP 2005-425452	20050622

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU

PRIORITY APPLN. INFO.:	EP 2005-425452	A	20050622
	US 2005-697398P	P	20050706

OTHER SOURCE(S): CASREACT 146:80528; MARPAT 146:80528

AB A process is described for the preparation of escitalopram and the pharmaceutically acceptable salts thereof starting from 5-cyanophthalide by a process which provides an enantioselective enzymic deacylation reaction of a complex of the formula (IV) where R represents a C1-C4 alkyl residue or an aryl residue under the action of an esterase from Aspergillus niger.

CC 16-2 (Fermentation and Bioindustrial Chemistry)

IT 481047-48-7
RL: BCP (Biochemical process); PCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(chemoenzymic process for synthesis of escitalopram)

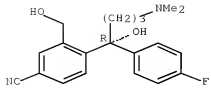
IT 128196-01-0P, Escitalopram
RL: IMF (Industrial manufacture); PRP (Properties); PUR (Purification or recovery); PREP (Preparation)
(chemoenzymic process for synthesis of escitalopram)

IT 481047-48-7
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(chemoenzymic process for synthesis of escitalopram)

RN 481047-48-7 HCAPLUS

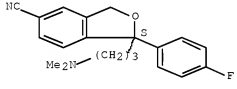
CN Benzonitrile, 4-[(1R)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 128196-01-0P, Escitalopram
RL: IMF (Industrial manufacture); PRP (Properties); PUR (Purification or recovery); PREP (Preparation)
(chemoenzymic process for synthesis of escitalopram)
RN 128196-01-0 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 7 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1316680 HCAPLUS Full-text
DOCUMENT NUMBER: 146:114862
TITLE: Interferon-induced depressive illness in hep C patients responds to SSRI antidepressant treatments
AUTHOR(S): Gupta, Ramesh K.; Kumar, Rajeev; Bassett, Mark
CORPORATE SOURCE: Consultation and Liaison Psychiatry, The Canberra Hospital, Garran, Australia
SOURCE: Neuropsychiatric Disease and Treatment (2006), 2(3), 355-358
CODEN: NDTEAZ; ISSN: 1176-6328
PUBLISHER: Dove Medical Press (NZ) Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This paper examines the role of selective serotonin reuptake inhibitors (SSRIs) in the treatment of hepatitis-C virus (HCV) patients who have developed interferon-α induced depression. A 2-yr data anal. of HCV psychiatric liaison clinic has been undertaken. The diagnosis, treatment, and progress of those patients who were treated with interferon-α (INF-α) are reported. 53 Of the 78 patients enrolled at the HCV Clinic and treated with INF-α were referred for psychiatric consultation. Six patients developed major depressive illness following INF therapy. They were all treated with SSRIs and they made full recovery. This is a significant observation and is concordant with other studies. Its biochem. ramifications are presented. It is concluded that INF-induced depression is fully reversible. A hypothesis is

proposed that SSRIs modulate the neuro-protective neurotoxic ratio by possibly inhibiting the indole-2,3-dioxygenase induction of the kynurenine pathway.

CC 1-11 (Pharmacology)

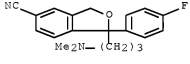
IT 5-HT reuptake inhibitors
Antidepressants
Hepatitis C
Hepatitis C virus
Human
(selective serotonin reuptake inhibitor was effective in recovery of interferon-α-induced depressive illness and may involve inhibition of indoleamine-2,3-dioxygenase induction of kynurenine pathway in hepatitis-C virus patient)

IT 59729-33-8, Citalopram
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SSRIs including citalopram was effective in recovery of interferon-α-induced depressive illness and may involve inhibition of indoleamine-2,3-dioxygenase induction of kynurenine pathway in hepatitis-C virus patient)

IT 59729-33-8, Citalopram
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SSRIs including citalopram was effective in recovery of interferon-α-induced depressive illness and may involve inhibition of indoleamine-2,3-dioxygenase induction of kynurenine pathway in hepatitis-C virus patient)

RN 59729-33-8 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)

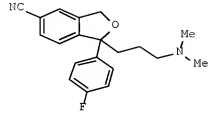


REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

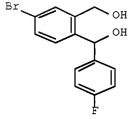
L38 ANSWER 8 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1176953 HCAPLUS Full-text
DOCUMENT NUMBER: 146:337723
TITLE: Process for the preparation of high purity citalopram and its pharmaceutically acceptable salts
INVENTOR(S): Muddasani, Pulla Reddy; Nannapaneni, Venkaiah Chowdary
PATENT ASSIGNEE(S): Natco Pharma Limited, India
SOURCE: Indian, 36pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 193430	A1	20040717	IN 2001-MA162	20010223

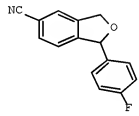
PRIORITY APPLN. INFO.: IN 2001-MA162 20010223
OTHER SOURCE(S): CASREACT 146:337723
GI



I



II



III

AB The invention relates to a process for the preparation of citalopram (I), which is a well-known antidepressant drug, and its hydrobromide salt as shown by the following example. Preparation of a Grignard reagent from 4-fluorobromobenzene followed by addition to 5-bromophthalide and reduction with NaBH4 gave diol II, which was taken directly to the next step without further purification Ring closure of II in the presence of catalytic 4-toluenesulfonic acid followed by substitution with copper(I) cyanide gave cyanophthalide III in 89% overall yield from the starting 5-bromophthalide. Compound III was deprotonated with dimsyl sodium in DMSO and alkylated with 3-(dimethylamino)propyl chloride to give citalopram (I) as the free base. The reaction was quenched with methanol, and then the reaction mixture was poured into water and extracted with toluene. The combined toluene layer was extracted with 20% aqueous acetic acid and the combined aqueous layers were neutralized with 25% aqueous ammonia to a pH of 7-7.5, whereupon the aqueous phase was extracted with diisopropyl ether. The organic layer was treated with carbon and filtered. The filtrate was partially concentrated and cooled to room temperature to give 74% yield of white citalopram crystals (99.5% purity). The free base of citalopram was suspended in diisopropyl ether and a solution of 48% HBr in acetic acid was added. After stirring for 2 h at room temperature, the reaction mixture was filtered and the solid was washed to give white crystalline citalopram hydrobromide in 88% yield (99.8% purity). The process of the invention allows for the preparation of pure grade citalopram base (>98.5% purity). Using 45% HBr in acetic acid allows for the convenient use of the required quantity of HBr on a com. scale and give highly pure citalopram hydrobromide (>99.8% purity) without any recrystn. process.

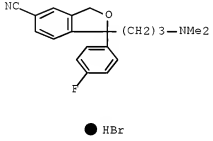
IC ICM C07D307-00
CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 45, 63
IT 59729-32-7P, Citalopram hydrobromide
RL: IMF (Industrial manufacture); PUR (Purification or recovery)

; SPN (Synthetic preparation); PREP (Preparation)
(target compound; process for the preparation of citalopram and its hydrobromide)

IT 59729-32-7P, Citalopram hydrobromide
RL: IMF (Industrial manufacture); PUR (Purification or recovery)
; SPN (Synthetic preparation); PREP (Preparation)
(target compound; process for the preparation of citalopram and its hydrobromide)

RN 59729-32-7 HCAPLUS

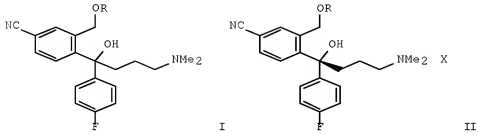
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



L38 ANSWER 9 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1065915 HCAPLUS Full-text
DOCUMENT NUMBER: 145:418932
TITLE: Process for the preparation of Escitalopram or its acid addition salts from racemic diol precursors by resolution and cyclization.
INVENTOR(S): Goankar, Santosh Laxman; Das, Prasenjit Prafulla; Narahari Babu, Ambati; Manjunatha, Sulur G.
PATENT ASSIGNEE(S): Jubilant Organosys Ltd., India
SOURCE: PCT Int. Appl., 25pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006106531	A1	20061012	WO 2006-IN124	20060404
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
IN 2005DE00856	A	20070105	IN 2005-DE856	20050404

PRIORITY APPLN. INFO.: IN 2005-DE856 A 20050404
OTHER SOURCE(S): MARPAT 145:418932
GI



AB A process for the preparation of highly pure Escitalopram or its acid addition salts comprises: (a) reaction of a racemic diol or ester derivative (I; R = H, ester forming group) with an optically active acid in ≥1 solvent to get enantiomerically pure diastereomer (II; R as before; X = optically active acid) (b) separating the enantiomerically pure diastereomer from its optically active acid salt by treating it with base and followed by stereoselective cyclization; (c) separating the Escitalopram base. Thus, 4-[4-(dimethylamino)-1-(4'-fluorophenyl)-1-hydroxy-1-butyl]-3-(hydroxymethyl)benzonitrile hydrobromide in H2O/PhMe was brought to pH 9-10 with 2M NaOH followed by separation and drying of the PhMe layer. PhMe was removed and the resulting oil was dissolved in MeOH/EtOH at 40-60° followed by addition of (+)-di-p-toluoyltartaric acid hydrate followed by cooling to 20-25°, stirring for 6-10 h, cooling to 0-5°, and filtering off the resulting solid to give (-)-4-[4-(dimethylamino)-1-(4'-fluorophenyl)-1-hydroxy-1-butyl]-3- (hydroxymethyl)benzonitrile hemi (+)-di-p-toluoyltartaric acid salt of >99% chiral purity. The latter in H2O/CH2Cl2 was treated with liquid ammonia; the CH2Cl2 layer was separated, washed with H2O, and dried. The solution was cooled and treated with Et3N and MeSO2Cl followed by stirring for 1 h at 20-25° to give Escitalopram base in >99% HPLC purity and >99.8% chiral purity.

CC 27-7 (Heterocyclic Compounds (One Hetero Atom))

IT 128196-01-0P, Escitalopram
RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of Escitalopram or its acid addition salts from racemic diol precursors by resolution and cyclization)

IT 219861-08-2P, Escitalopram oxalate
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation of Escitalopram or its acid addition salts from racemic diol precursors by resolution and cyclization)

IT 912452-31-4P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of Escitalopram or its acid addition salts from racemic diol precursors by resolution and cyclization)

IT 109-54-6, 3-Dimethylaminopropyl chloride 460-00-4, 4-Fluorobromobenzene

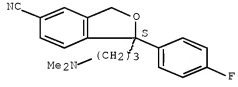
82104-74-3, 5-Cyanophthalide 103146-26-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of Escitalopram or its acid addition salts from racemic diol precursors by resolution and cyclization)

IT 128196-01-0P, Escitalopram
RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of Escitalopram or its acid addition salts from racemic diol precursors by resolution and cyclization)

RN 128196-01-0 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 219861-08-2P, Escitalopram oxalate
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation of Escitalopram or its acid addition salts from racemic diol precursors by resolution and cyclization)

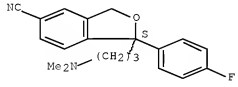
RN 219861-08-2 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1), (1S)- (CA INDEX NAME)

CM 1

CRN 128196-01-0
CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (+).



CM 2

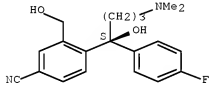
CRN 144-62-7
CMF C2 H2 O4

IT 912452-31-4P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of Escitalopram or its acid addition salts from racemic diol precursors by resolution and cyclization)
RN 912452-31-4 HCAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with 4-[(1S)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 488787-59-3
CMF C20 H23 F N2 O2

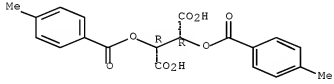
Absolute stereochemistry. Rotation (-).



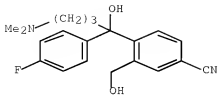
CM 2

CRN 32634-66-5
CMF C20 H18 O8

Absolute stereochemistry. Rotation (-).



IT 103146-26-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of Escitalopram or its acid addition salts from racemic diol precursors by resolution and cyclization)
RN 103146-26-5 HCAPLUS
CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)-, hydrobromide (1:1) (CA INDEX NAME)



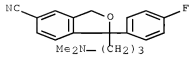
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 10 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:64209 HCAPLUS Full-text
DOCUMENT NUMBER: 144:135523
TITLE: Chiral separation and quantitative analysis of citalopram by capillary electrophoresis with dextrin as chiral additive
AUTHOR(S): Xiao, Shangyou; Xu, Hongmei; Tang, Shouyuan; Feng, Bo; Tao, Ran; Ying, Yongguang; Xia, Zhining
CORPORATE SOURCE: Key Lab. Biomechanics & Tissue Eng. State Education Ministry of China, Dep. Pharmaceutics, Coll. Chem. Chem. Eng., Chongqing Univ., Chongqing, 400044, Peop. Rep. China
SOURCE: Fenxi Huaxue (2005), 33(11), 1527-1530
CODEN: FHHHDT; ISSN: 0253-3820
PUBLISHER: Kexue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Citalopram (CIT) was separated by capillary electrophoresis using dextrin as chiral additive. The effect of the concentration of dextrin, pH, concentration of electrophoretic running buffer and separation voltage were investigated. The optimized conditions were obtained with 20 kV as separation voltage, 7.0% (m/V) dextrin in 80 mmol/L phosphate(pH 5.4) as running buffer. Good resolution of citalopram enantiomers was achieved and the Rs was 3.9 under optimal conditions. The mechanism of separation was discussed too. The quant. anal. of citalopram was investigated. The linear range of concentration of R-(-)-CIT was 0.05.apprx.4.00 g/L. The limit of detection of two enantiomers was 25.3 mg/L and 27.3 mg/L. The correlation coefficient was more than 0.9970, and the RSD was no more than 3.2% resp.

CC 64-3 (Pharmaceutical Analysis)
IT 59729-33-8P, Citalopram
RL: ANT (Analyte); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chiral separation and quant. anal. of citalopram by capillary electrophoresis with dextrin as chiral additive)
IT 59729-33-8P, Citalopram
RL: ANT (Analyte); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chiral separation and quant. anal. of citalopram by capillary electrophoresis with dextrin as chiral additive)

RN 59729-33-8 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



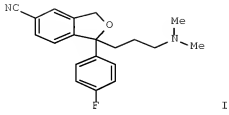
L38 ANSWER 11 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1004542 HCAPLUS Full-text
DOCUMENT NUMBER: 143:311965
TITLE: Crystalline composition containing escitalopram oxalate
INVENTOR(S): Jensen, Kim Bojstrup; Humble, Rikke Eva; Liljegren, Ken; Christensen, Troels Volsgaard
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005084643	A1	20050915	WO 2005-DK115	20050221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005218713	A1	20050915	AU 2005-218713	20050221
CA 2558198	A1	20050915	CA 2005-2558198	20050221
EP 1732514	A1	20061220	EP 2005-706777	20050221
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
CN 1925844	A	20070307	CN 2005-80006940	20050221
BR 2005008266	A	20070731	BR 2005-8266	20050221
JP 2007526262	T	20070913	JP 2007-501117	20050221
MX 2006PA09976	A	20061115	MX 2006-PA9976	20060904
IN 2006CN03227	A	20070706	IN 2006-CN3227	20060905
NO 2006004499	A	20061204	NO 2006-4499	20061004

PRIORITY APPLN. INFO.:

DK 2004-382	A	20040305
US 2004-550909P	P	20040305
WO 2005-DK115	W	20050221

GI



I

AB The present invention discloses crystalline particles of escitalopram oxalate (S-I oxalate) which either have a broad particle size distribution or comprise at least 0.01 % (weight/weight) of Z-4-(4-dimethylamino-1-(4- fluorophenyl)-but-1-enyl)-3-hydroxymethylbenzonitrile (II), said particles being suitable for use in direct compression. Furthermore, the invention discloses a novel pharmaceutical unit dosage form containing such crystalline particles of S-I oxalate as well as methods for manufacture of such crystalline particles of escitalopram oxalate. Finally, the invention provides a method for reduction of the amount of hydroxyl containing impurities in a solution of I or S-I. The hydroxyl impurity II was scavenged by succinic anhydride.

IC ICM A61K009-14
ICS A61K031-34; A61P025-24

CC 63-6 (Pharmaceuticals)

IT 219861-08-2P, Escitalopram oxalate
RL: PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystalline composition containing escitalopram oxalate)

IT 481047-48-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(crystalline composition containing escitalopram oxalate)

IT 219861-08-2P, Escitalopram oxalate
RL: PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystalline composition containing escitalopram oxalate)

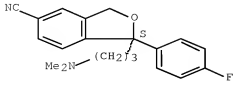
RN 219861-08-2 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1), (1S)- (CA INDEX NAME)

CM 1

CRN 128196-01-0
CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (+).

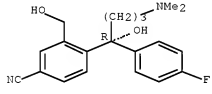


CM 2

CRN 144-62-7
CMF C2 H2 O4

IT 481047-48-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(crystalline composition containing escitalopram oxalate)
RN 481047-48-7 HCAPLUS
CN Benzonitrile, 4-[(1R)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 12 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:983778 HCAPLUS Full-text
DOCUMENT NUMBER: 143:272423
TITLE: Crystalline composition containing escitalopram
INVENTOR(S): Jensen, Kim Bojstrup; Humble, Rikke Eva; Liljegren, Ken; Christensen, Troels Volsgaard
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: U.S. Pat. Appl. Publ., 9 pp., Division of U.S. Ser. No. 851,763.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005197388	A1	20050908	US 2004-948594		20040923
US 2005196453	A1	20050908	US 2004-851763		20040521
PRIORITY APPLN. INFO.:			US 2004-550909P	P	20040305
			US 2004-851763	A3	20040521

AB The present invention discloses crystalline particles of escitalopram oxalate which either have a broad particle size distribution or comprise at least 0.01% (weight/weight) of Z-4-(4-dimethylamino-1-(4-fluorophenyl)-but-1-enyl)-3- hydroxymethyl-benzonitrile, said particles being suitable for use in direct compression. Furthermore, the invention discloses a novel pharmaceutical unit dosage form containing such crystalline particles of escitalopram oxalate as well as methods for manufacture of such crystalline particles of escitalopram oxalate. Finally, the invention provides a method for reduction of the amount of hydroxyl containing impurities in a solution of citalopram or escitalopram.

IC ICM A61K031-343
ICS A61K009-14

INCL 514469000; 424489000; 549467000

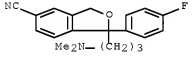
CC 63-5 (Pharmaceuticals)

IT 59729-33-8P, Citalopram 128196-01-0P, Escitalopram 219861-08-2P, Escitalopram oxalate
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tablets made from crystalline particles of escitalopram oxalate purified by anhydrides)

IT 59729-33-8P, Citalopram 128196-01-0P, Escitalopram 219861-08-2P, Escitalopram oxalate
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tablets made from crystalline particles of escitalopram oxalate purified by anhydrides)

RN 59729-33-8 HCAPLUS

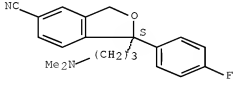
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



RN 128196-01-0 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



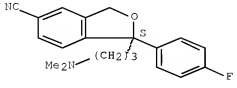
RN 219861-08-2 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1), (1S)- (CA INDEX NAME)

CM 1

CRN 128196-01-0
CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (+).



CM 2

CRN 144-62-7
CMF C2 H2 O4

L38 ANSWER 13 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:902848 HCAPLUS Full-text
DOCUMENT NUMBER: 143:248161
TITLE: Method for the separation of intermediates which may be used for the preparation of escitalopram
INVENTOR(S): Lyngso, Lars Ole
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005077891	A1	20050825	WO 2005-DK75	20050202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005212455	A1	20050825	AU 2005-212455	20050202

CA 2555980	A1	20050825	CA 2005-2555980		20050202
EP 1716108	A1	20061102	EP 2005-700625		20050202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU					
CN 1918112	A	20070221	CN 2005-80004594		20050202
BR 2005007580	A	20070731	BR 2005-7580		20050202
JP 2007524678	T	20070830	JP 2006-552461		20050202
MX 2006PA08977	A	20061020	MX 2006-PA8977		20060808
IN 2006CN02945	A	20070608	IN 2006-CN2945		20060810
NO 2006004086	A	20060912	NO 2006-4086		20060912
US 2007190624	A1	20070816	US 2006-597836		20061108
PRIORITY APPLN. INFO.:			DK 2004-217	A	20040212
			US 2004-544970P	P	20040212
			WO 2005-DK75	W	20050202

OTHER SOURCE(S): CASREACT 143:248161; MARPAT 143:248161
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Compds. I [R1 = H, or group II; R2 = CN, or a group which may be converted to CN; R3 = halo; X = double or single bond; Y = bond, O, S, or NH; W = O, or S; R4 = alkyl, alkenyl, alkynyl, aryl, hetroaryl, all of which may be optionally substituted with alkoxy, alkythio, halo, OH, NH, NO2, CN, alkylamino, aryl, aryloxy, arylthio, and heteroaryl], or a salt from a mixture of I [R1 = group II] and I [R1 = H], which was reacting with cyclic anhydride or imide to form a mixture of I [R1 = group II] and an esters III (R5 = substituted heteroaryl carboxylic acid), were prepared by enzymic acylation or deacylation, separated, isolated and purified and used for manufacturing of escitalopram and derivs. Compds. I [R1 = group II] were separated from esters III by precipitation of III from the mixture, or by partitioning between an organic solvent and aqueous solvent, by adsorbing I [R1 = group II] on a basic resin. Thus, addition of succinic anhydride to a mixture of butyric acid 5-cyano-2-[4-dimethylamino-1-(4-fluorophenyl)-1-hydroxybutyl]-benzyl ester and prepared by enzymic resolution 4-[(S)-4-dimethylamino-1-(4'-fluorophenyl)-1-hydroxybutyl]-3-hydroxymethylbenzonitrile, gave after precipitation and washing 2,02 g of escitalopram [(S)-1-(3-dimethylamino-propyl)-1-(4-fluoro-phenyl)- 1,3-dihydro-isobenzofuran-5-carbonitrile] hydrogen oxalate (ee = 95%).

IC ICM C07C253-34
ICS C07C253-30; C07C255-59; C07D307-87

CC 25-20 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 7

IT 219861-08-2P, Escitalopram
RL: BPN (Biosynthetic preparation); IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation by enzymic acylation or deacylation, separation, isolation and purification by precipitation, partitioning, or adsorption, of benzonitriles used as intermediates for synthesis of escitalopram and derivs.)

IT 488787-59-3P 863116-45-4P
RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation by enzymic acylation or deacylation, separation, isolation and

purification by precipitation, partitioning, or adsorption, of benzonitriles used as
intermediates for synthesis of escitalopram and derivs.)

IT 108-30-5, Succinic anhydride, reactions 103146-25-4 658080-70-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation by enzymic acylation or deacylation, separation, isolation and purification by precipitation, partitioning, or adsorption, of benzonitriles used as
intermediates for synthesis of escitalopram and derivs.)

IT 219861-08-2P, Escitalopram
RL: BPN (Biosynthetic preparation); IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation by enzymic acylation or deacylation, separation, isolation and purification by precipitation, partitioning, or adsorption, of benzonitriles
used as intermediates for synthesis of escitalopram and derivs.)

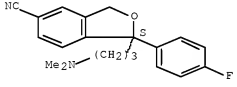
RN 219861-08-2 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1), (1S)- (CA INDEX NAME)

CM 1

CRN 128196-01-0
CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (+).



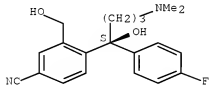
CM 2

CRN 144-62-7
CMF C2 H2 O4

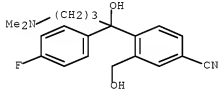
IT 488787-59-3P
RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation by enzymic acylation or deacylation, separation, isolation and purification by precipitation, partitioning, or adsorption, of

benzonitriles used as
intermediates for synthesis of escitalopram and derivs.)
RN 488787-59-3 HCAPLUS
CN Benzonitrile, 4-[(1S)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 103146-25-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation by enzymic acylation or deacylation, separation, isolation and purification by precipitation, partitioning, or adsorption, of
benzonitriles used as
intermediates for synthesis of escitalopram and derivs.)
RN 103146-25-4 HCAPLUS
CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 14 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:780979 HCAPLUS Full-text
DOCUMENT NUMBER: 144:115
TITLE: Liquid-phase microextraction of basic drugs - selection of extraction mode based on computer calculated solubility data
AUTHOR(S): Pedersen-Bjergaard, Stig; Rasmussen, Knut Einar; Brekke, Anders; Ho, Tung Si; Halvorsen, Trine Gronhaug
CORPORATE SOURCE: School of Pharmacy, University of Oslo, Oslo, Norway
SOURCE: Journal of Separation Science (2005), 28(11), 1195-1203
CODEN: JSSCCJ; ISSN: 1615-9306
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The extractability of 58 different basic drugs by 3-phase liquid-phase microextn. (LPME) was studied. Extraction recoveries were correlated to

solubility data and log D data calculated with a com. computer program. The basic drugs were extracted from 1.5 mL water samples (pH 13) through approx. 15 μL of dodecyl acetate immobilized within the pores of a porous polypropylene hollow fiber (organic phase), and into 15 μL of 10 mM HCl (acceptor solution) present inside the lumen of the hollow fiber. Compds. with a calculated solubility below 1 mg/mL at pH 2 were poorly recovered and remained principally in the organic phase. For these drugs, 2-phase LPME may be used as an alternative technique, where the aqueous acceptor phase is replaced by an organic solvent. In the solubility range 1-5 mg/mL, most drugs were effectively extracted (recovery >30%), whereas drugs belonging to the solubility range 5-150 mg/mL were all extracted with recoveries above 30% by 3-phase LPME. The hydrophilic nature of most drugs with solubilities above 150 mg/mL prevented them from entering the organic phase, and only those with log D >1.8 were effectively recovered by 3-phase LPME. For drugs with log D < 1.8 (and solubility > 150 mg/mL), carrier-mediated LPME was found to be the preferred technique, where an ion-pair reagent (octanoic acid) was added to the sample. In the case of carrier-mediated LPME, the volume of sample was decreased to 100 μL to facilitate rapid extns. Based on the present work, the extractability of new compds. may easily be predicted to speed up method development. Extns. were also accomplished from plasma samples, where interactions between proteins and the drugs may reduce the extraction recovery. However, dilution of the plasma samples with water and adjustment of pH into the alkaline region effectively suppressed drug-protein interactions for most of the drugs studied.

CC 1-1 (Pharmacology)
Section cross-reference(s): 64

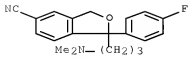
IT 50-48-6P, Amitriptyline 50-52-2P, Thioridazine 50-53-3P, Chlorpromazine, analysis 50-55-5P, Reserpine 52-53-9P, Verapamil 52-86-8P, Haloperidol 57-42-1P, Pethidine 58-38-8P, Prochlorperazine 58-39-9P, Perphenazine 58-73-1P, Diphenhydramine 60-87-7P, Promethazine 60-99-1P, Levomepromazine 69-23-8P, Fluphenazine 72-69-5P, Nortriptyline 76-57-3P, Codeine 76-99-3P, Methadone 82-93-9P, Chlorcyclizine 86-54-4P, Hydralazine 91-84-9P, Mepyramine 113-59-7P, Chlorprothixene 137-58-6P, Lidocaine 300-62-9P, Amphetamine 303-49-1P, Clomipramine 525-66-6P, Propranolol 537-46-2P, Methamphetamine 569-65-3P, Meclizine 739-71-9P, Trimipramine 1668-19-5P, Doxepin 2062-78-4P, Pimozide 2470-73-7P, Dixyrazine 3930-20-9P, Sotalol 5786-21-0P, Clozapine 6673-35-4P, Practolol 14838-15-4P, Phenylpropanolamine 15686-51-8P, Clemastine 24219-97-4P, Mianserin 26839-75-8P, Timolol 29122-68-7P, Atenolol 34911-55-2P, Amfebutamon 42399-41-7P, Diltiazem 50679-08-8P, Terfenadine 51481-61-9P, Cimetidine 53179-11-6P, Loperamide 53772-83-1P, Zuclopenthixol 54739-18-3P, Fluvoxamine 54910-89-3P, Fluoxetine 59729-33-8P, Citalopram 61869-08-7P, Paroxetine 66357-35-5P, Ranitidine 71320-77-9P, Moclobemide 71620-89-8P, Reboxetine 79617-96-2P, Sertraline 83366-66-9P, Nefazodone 93413-69-5P, Venlafaxine 106266-06-2P, Risperidone 111974-69-7P, Quetiapine 132539-06-1P, Olanzapine
RL: ANT (Analyte); PUP (Purification or recovery); ANST (Analytical study); PREP (Preparation)
(liquid-phase microextn. of basic drugs using selection of extraction mode based on computer-calculated solubility data)

IT 59729-33-8P, Citalopram
RL: ANT (Analyte); PUR (Purification or recovery); ANST (Analytical study); PREP (Preparation)
(liquid-phase microextn. of basic drugs using selection of extraction mode based on computer-calculated solubility data)

RN 59729-33-8 HCAPLUS

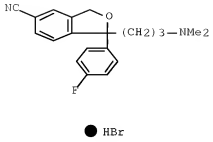
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-

fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 15 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:529087 HCAPLUS Full-text
DOCUMENT NUMBER: 143:393263
TITLE: Chiral Separation of Citalopram Hydrobromide Enantiomers and ee of Escitalopram Oxalate
AUTHOR(S): Pan, Hongjuan; Zhu, Xueyan
CORPORATE SOURCE: Shanghai Institute of Pharmaceutical Industry, Shanghai, 200040, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (2004), 35(8), 484-485
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB An HPLC method for chiral separation of citalopram hydrobromide enantiomers and optical purity detection of escitalopram oxalate was established. A Chiralpak AD-H chiral column was used with the mobile phase of n-hexane-isopropylalc.-diethylamine (95:5:0.1). The column temperature was 25 degree C, and the detection wavelength was 240 nm. The average resolution between S-(+)-and R-(-)-citalopram was 2.47. The R-(-)-citalopram content was less than 1.0. The ee of escitalopram oxalate was more than 98.0%.
CC 64-3 (Pharmaceutical Analysis)
IT 59729-32-7P, Citalopram hydrobromide 219861-08-2P, Escitalopram oxalate
RL: ANT (Analyte); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chiral separation of citalopram hydrobromide enantiomers and ee of escitalopram oxalate)
IT 59729-32-7P, Citalopram hydrobromide 219861-08-2P, Escitalopram oxalate
RL: ANT (Analyte); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chiral separation of citalopram hydrobromide enantiomers and ee of escitalopram oxalate)
RN 59729-32-7 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)

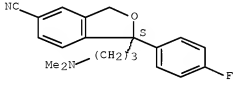


RN 219861-08-2 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1), (1S)- (CA INDEX NAME)

CM 1

CRN 128196-01-0
CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (+).



CM 2

CRN 144-62-7
CMF C2 H2 O4

L38 ANSWER 16 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:526516 HCAPLUS Full-text
DOCUMENT NUMBER: 143:339414
TITLE: Effects of acute and long-term administration of escitalopram and citalopram on serotonin neurotransmission: an in vivo electrophysiological study in rat brain
AUTHOR(S): El Mansari, Mostafa; Sanchez, Connie; Chouvet, Guy; Renaud, Bernard; Haddjeri, Nasser
CORPORATE SOURCE: Laboratory of Neuropharmacology and Neurochemistry, Faculty of Pharmacy, University of Claude Bernard Lyon

I, Lyon, Fr.
SOURCE: Neuropsychopharmacology (2005), 30(7), 1269-1277
CODEN: NEROEW; ISSN: 0893-133X
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study was undertaken to compare the acute and long-term effects of escitalopram and citalopram on rat brain 5-HT neurotransmission, using electrophysiol. techniques. In hippocampus, after 2 wk of treatment with escitalopram (10 mg/kg/day, s.c.) or citalopram (20 mg/kg/day, s.c.), the administration of the selective 5-HT1A receptor antagonist WAY-100,635 (20-100 μg/kg, i.v.) dose-dependently induced a similar increase in the firing activity of dorsal hippocampus CA3 pyramidal neurons, thus revealing direct functional evidence of an enhanced tonic activation of postsynaptic 5-HT1A receptors. In dorsal raphe nucleus, escitalopram was four times more potent than citalopram in suppressing the firing activity of presumed 5-HT neurons (ED50 = 58 and 254 μg/kg, i.v., resp.). Interestingly, the suppressant effect of escitalopram (100 μg/kg, i.v.) was significantly prevented, but not reversed by R-citalopram (250 μg/kg, i.v.). Sustained administration of escitalopram and citalopram significantly decreased the spontaneous firing activity of presumed 5-HT neurons. This firing activity returned to control rate after 2 wk in rats treated with escitalopram, but only after 3 wk using citalopram, and was associated with a desensitization of somatodendritic 5-HT1A autoreceptors. These results suggest that the time course of the gradual return of presumed 5-HT neuronal firing activity, which was reported to account for the delayed effect of SSRI on 5-HT transmission, is congruent with the earlier onset of action of escitalopram vs citalopram in validated animal models of depression and anxiety.

CC 1-11 (Pharmacology)

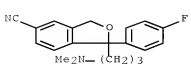
IT 5-HT reuptake inhibitors
Neurotransmission
(long term treatment of SSRI escitalopram, citalopram suppressed activity of 5-HT neurons followed by recovery and was associated with desensitization of somatodendritic 5-HT1A autoreceptor in brain of rat)

IT 59729-33-8, Citalopram 128196-01-0, Escitalopram
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(long term treatment of SSRI escitalopram, citalopram suppressed activity of 5-HT neurons followed by recovery and was associated with desensitization of somatodendritic 5-HT1A autoreceptor in brain of rat)

IT 59729-33-8, Citalopram 128196-01-0, Escitalopram
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(long term treatment of SSRI escitalopram, citalopram suppressed activity of 5-HT neurons followed by recovery and was associated with desensitization of somatodendritic 5-HT1A autoreceptor in brain of rat)

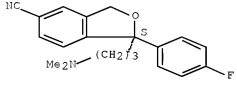
RN 59729-33-8 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



RN 128196-01-0 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 17 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:135410 HCAPLUS Full-text
DOCUMENT NUMBER: 142:219139
TITLE: Method for the preparation of citalopram via a magnesium-salt intermediate prepared by the Grignard reaction of 4-fluorophenylmagnesium bromide and 3-dimethylaminopropylmagnesium chloride with 5-cyanophthalide
INVENTOR(S): Cotticelli, Giovanni; Di Lernia, Gianluca; Silvia, Milanesi
PATENT ASSIGNEE(S): Adorkem Technology Spa, Italy
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1506963	A1	20050216	EP 2003-425693	20031028
EP 1506963	B1	20050413		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 293106	T	20050415	AT 2003-425693	20031028
ES 2240931	T3	20051016	ES 2003-3425693	20031028
CA 2543155	A1	20050602	CA 2004-2543155	20041022
WO 2005049595	A1	20050602	WO 2004-EP52626	20041022
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,				

SN, TD, TG

EP 1682526	A1	20060726	EP 2004-791287		20041022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
CN 1875013	A	20061206	CN 2004-80031662		20041022
BR 2004015778	A	20061226	BR 2004-15778		20041022
JP 2007511477	T	20070510	JP 2006-537287		20041022
HK 1075041	A1	20060721	HK 2005-107094		20050816
IN 2006DN02249	A	20070713	IN 2006-DN2249		20060424
MX 2006PA04568	A	20060720	MX 2006-PA4568		20060425
US 2007060759	A1	20070315	US 2006-577869		20060623
PRIORITY APPLN. INFO.:			EP 2003-425693	A	20031028
			WO 2004-EP52626	W	20041022

OTHER SOURCE(S): CASREACT 142:219139; MARPAT 142:219139

AB A method for the preparation of citalopram and its pharmaceutically acceptable salts is described; its obtained starting from 5-cyanophthalide by its Grignard reaction with a mixture of 4-fluorophenylmagnesium bromide and 3-dimethylaminopropylmagnesium chloride to give a chloro- or bromomagnesium-salt intermediate. The chloro- or bromomagnesium-salt intermediate obtained is then subjected to intramol. cyclocondensation without isolation using either an organic or inorg. acid (e.g., 85% ortho-phosphoric acid) to give citalopram.

IC ICM C07D307-87
ICS C07C255-50; C07F003-02

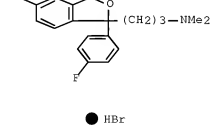
CC 27-7 (Heterocyclic Compounds (One Hetero Atom))

IT 59729-32-7P, Citalopram hydrobromide
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(method for preparation of citalopram via magnesium-salt intermediate prepared by Grignard reaction of 4-fluorophenylmagnesium bromide and 3-dimethylaminopropylmagnesium chloride with 5-cyanophthalide)

IT 59729-32-7P, Citalopram hydrobromide
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(method for preparation of citalopram via magnesium-salt intermediate prepared by Grignard reaction of 4-fluorophenylmagnesium bromide and 3-dimethylaminopropylmagnesium chloride with 5-cyanophthalide)

RN 59729-32-7 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



● HBr

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 18 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:120910 HCAPLUS Full-text
DOCUMENT NUMBER: 142:197860
TITLE: Process for purification of citalopram via washing with polybasic acid solutions
INVENTOR(S): Uttarwar, Sunil Govindrao; Gawli, Bhagwan Narayan
PATENT ASSIGNEE(S): Meditab Specialities Pvt. Ltd., India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005012278	A2	20050210	WO 2004-GB3209	20040723
WO 2005012278	A3	20050616		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
GB 2418916	A	20060412	GB 2006-1023	20040723
GB 2418916	B	20071107		
DE 112004001368	T5	20060629	DE 2004-112004001368	20040723
IN 2006MN00092	A	20061006	IN 2006-MN92	20060124
US 2006189816	A1	20060824	US 2006-565736	20060419
PRIORITY APPLN. INFO.:			GB 2003-17475 A	20030725
			WO 2004-GB3209 W	20040723

OTHER SOURCE(S): CASREACT 142:197860

AB A process for purification of racemic or optically active citalopram (I) comprises (i) providing crude I containing ≥1 I derivs. dissolved in a H2O-immiscible organic solvent, (ii) washing the crude mixture with ≥1 dilute aqueous solution of a polybasic acid, either in free form or as a partial alkali metal salt, so as to sep. I from impurities present in the crude mixture; and (iii) where required converting purified I free base to a pharmaceutically acceptable salt. Thus, 4-[4-(dimethylamino)-1-(4'-fluorophenyl)-1-hydroxybutyl]-3-hydroxymethylbenzonitrile was heated at 105° in aqueous H3PO4 followed by cooling, dilution with H2O, pH adjustment to 8-10 with aqueous NH3, and extraction with EtOAc. The EtOAc layer was washed with aqueous disodium edetate followed by drying over Na2SO4, treatment with decolorizing C, and filtration to give >99.85% pure citalopram hydrobromide.

IC ICM C07D307-00
CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
IT 5-HT reuptake inhibitors
(process for purification of citalopram)
IT 59729-33-8P, Citalopram
RL: PAC (Pharmacological activity); PUP (Purification or recovery); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for purification of citalopram)

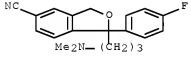
IT 59729-32-7P, Citalopram hydrobromide
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for purification of citalopram via washing with polybasic acid solns.)

IT 60-00-4, Edetic acid, reactions 77-92-9, Citric acid, reactions 87-69-4, Tartaric acid, reactions 110-17-8, Fumaric acid, reactions 124-63-0, Methanesulfonyl chloride 139-33-3 144-62-7, Oxalic acid, reactions 64169-39-7 103146-25-4 488787-59-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for purification of citalopram via washing with polybasic acid solns.)

IT 128196-01-0P, Escitalopram
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for purification of citalopram via washing with polybasic acid solns.)

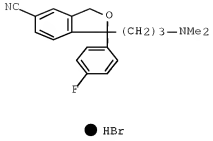
IT 59729-33-8P, Citalopram
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for purification of citalopram)

RN 59729-33-8 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)

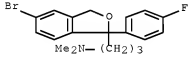


IT 59729-32-7P, Citalopram hydrobromide
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for purification of citalopram via washing with polybasic acid solns.)

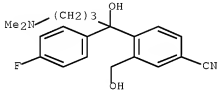
RN 59729-32-7 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



IT 64169-39-7 103146-25-4 488787-59-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for purification of citalopram via washing with polybasic acid solns.)
RN 64169-39-7 HCAPLUS
CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (CA INDEX NAME)

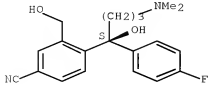


RN 103146-25-4 HCAPLUS
CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



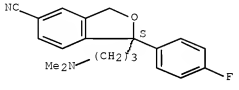
RN 488787-59-3 HCAPLUS
CN Benzonitrile, 4-[(1S)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 128196-01-0P, Escitalopram
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for purification of citalopram via washing with polybasic acid solns.)
RN 128196-01-0 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L38 ANSWER 19 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:119195 HCAPLUS Full-text
DOCUMENT NUMBER: 142:312437
TITLE: Purification and fluorescent labeling of the human serotonin transporter
AUTHOR(S): Rasmussen, Soren G. F.; Gether, Ulrik
CORPORATE SOURCE: Molecular Neuropharmacology Group, Department of Pharmacology, Panum Institute, University of Copenhagen, Copenhagen, DK-2200, Den.
SOURCE: Biochemistry (2005), 44(9), 3494-3505
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To establish a purification procedure for the human serotonin transporter (hSERT) we expressed in Sf9 insect cells an epitope-tagged version of the transporter containing a FLAG epitope at the N-terminus and a polyhistidine tail at the C-terminus (FLAG-hSERT-12H). For purification, the transporter was solubilized in digitonin followed by nickel affinity and subsequent Con A chromatog. Using this procedure we were able to obtain an overall purification of 700-fold and a yield of .apprx.0.1 mg/L of cell culture. The purified transporter displayed pharmacol. properties similar to those of hSERT expressed in native tissues and in transfected cell lines. Fluorescent labeling of the purified transporter with the thiol-reactive fluorophore nitrobenxoxadiazol-iodoacetamide (IANBD) and Texas Red bromoacetamide preserved the pharmacol. profile of FLAG-hSERT-12H. Collisional quenching expts. revealed that the aqueous quencher iodide was able to cause marked quenching of the fluorescence of the IANBD labeled transporter with a KSV of 3.4±0.10 M-1. In a mutant transporter with five cysteines mutated (5CysKO) we observed a significant reduction in this quenching (KSV = 2.1±0.16 M-1, p < 0.01). This reduction was most likely due to labeling of 109Cys since mutation of this cysteine alone resulted in a reduction in collisional quenching that was similar to that observed with 5CysKO (KSV = 2.2±0.15 M-1). These data suggest that labeling of 109Cys contributes substantially to the overall fluorescence of IANBD labeled FLAG-hSERT-12H. On the basis of these

data we infer that 109Cys is embedded in a mixed hydrophobic/hydrophilic environment at the external ends of transmembrane segments 1 and 2. Further use of fluorescent techniques on purified hSERT should prove useful in future studies aimed at understanding the mol. structure and function of Na+/Cl-- dependent neurotransmitter transporters.

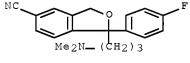
CC 9-5 (Biochemical Methods)
Section cross-reference(s): 2

IT 50-36-2, Cocaine 50-49-7, Imipramine 59729-33-8, Citalopram 135416-43-2, RTI-55
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(purification and fluorescent labeling of human serotonin transporter)

IT 59729-33-8, Citalopram
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(purification and fluorescent labeling of human serotonin transporter)

RN 59729-33-8 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)

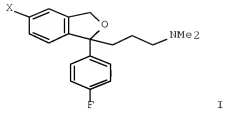


REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

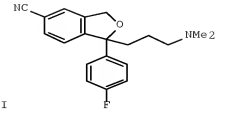
L38 ANSWER 20 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1079731 HCAPLUS Full-text
DOCUMENT NUMBER: 142:56160
TITLE: process for purification of citalopram by hydrogenolysis halogenated isobenzofuran impurities
INVENTOR(S): Borase, Ashok Punju; Patel, Nileshkumar Sureshbai; Kilaru, Srinivasu; Thennati, Rajamannar
PATENT ASSIGNEE(S): Sun Pharmaceuticals Industries Ltd., India
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1486492	A2	20041215	EP 2004-291424	20040608
EP 1486492	A3	20050223		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
IN 2003MU00602	A	20050211	IN 2003-MU602	20030610
US 2005004380	A1	20050106	US 2004-865139	20040608
US 7019153	B2	20060328		
PRIORITY APPLN. INFO.:			IN 2003-MU602 A	20030610

OTHER SOURCE(S): MARPAT 142:56160
GI



I



II

AB The present invention provides a process for decreasing the content of halogenated isobenzofuran impurities I (X = halo) in citalopram (II) by hydrogenolysis to I (X = H). Thus, 5 g crude citalopram base containing 4.84% of bromo impurity I (X = Br) is dissolved in 50 mL EtOAc, 0.1 g Pd/C and 0.1 g sodium hypophosphite added and the mixture refluxed for 2 h. Anal. showed that the bromo impurity I (X = Br) is absent.

IC ICM C07D307-87

CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 63

IT 59729-32-7P, Citalopram hydrobromide 59729-33-8P,
Citalopram 207559-01-1P, Citalopram oxalate
RL: PUR (Purification or recovery); PREP (Preparation)
(process for purification of citalopram by hydrogenolysis halogenated impurities)

IT 64169-39-7
RL: RCT (Reactant); REM (Removal or disposal); PROC (Process); RACT (Reactant or reagent)
(process for purification of citalopram by hydrogenolysis halogenated impurities)

IT 59729-32-7P, Citalopram hydrobromide 59729-33-8P,
Citalopram 207559-01-1P, Citalopram oxalate
RL: PUR (Purification or recovery); PREP (Preparation)
(process for purification of citalopram by hydrogenolysis halogenated impurities)

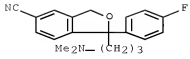
RN 59729-32-7 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)

● HBr

RN 59729-33-8 HCAPLUS

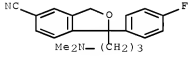
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



RN 207559-01-1 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1) (CA INDEX NAME)

CM 1

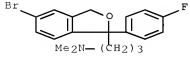
CRN 59729-33-8
CMF C20 H21 F N2 O



CM 2

CRN 144-62-7
CMF C2 H2 O4

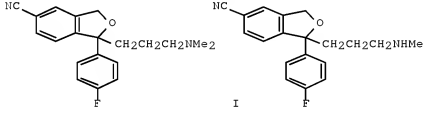
IT 64169-39-7
RL: RCT (Reactant); REM (Removal or disposal); PROC (Process); PACT (Reactant or reagent)
(process for purification of citalopram by hydrogenolysis halogenated impurities)
RN 64169-39-7 HCAPLUS
CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (CA INDEX NAME)



L38 ANSWER 21 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:691476 HCAPLUS Full-text
DOCUMENT NUMBER: 141:207048
TITLE: Preparation of pure citalopram
INVENTOR(S): Kaushik, Vipin Kumar; Rao, Divvela Venkata Naga Srinivasa; Handa, Vijay Kumar; Sivakumaran, Meenakshisunderam
PATENT ASSIGNEE(S): Aurobindo Pharma Ltd., India
SOURCE: U.S., 3 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

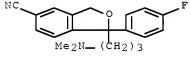
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6781003	B1	20040824	US 2003-456135	20030609
PRIORITY APPLN. INFO.:			US 2003-456135	20030609

OTHER SOURCE(S): CASREACT 141:207048
GI

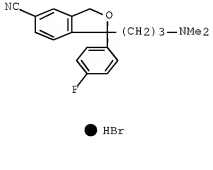


AB The present invention relates to an industrially advantageous method for the purification of citalopram (I) wherein desmethyl citalopram (II), present in crude citalopram as an impurity, is methylated to produce pure citalopram I. The resulting citalopram product I is isolated as the base or a pharmaceutically acceptable salt thereof. Thus, to crude citalopram (90 g, 0.28 mol) containing desmethyl citalopram (7 %, HPLC), formic acid (98%, 2.7 g) was added followed by aqueous formaldehyde(35%, 2.37 g). The reaction mass was heated at 85-95° for 30 min, cooled to 30°, and diluted with ethanol (900 mL), treated with oxalic acid dihydrate (41.94 g, 0.33 mol), and heated to reflux. The obtained solution was cooled to 20-25° and stirring was continued for 2 h at 20-25°, followed by collecting the product by filtration and recrystn. from ethanol to give highly pure 92 g crystalline citalopram oxalate having HPLC purity 99.7% wherein desmethyl citalopram (impurity) was not detected.
IC ICM C07D307-78
INCL 549467000; 549469000
CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
IT 59729-33-8P, Citalopram
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation of pure citalopram by N-methylation of crude citalopram containing
desmethyl citalopram with formaldehyde and formic acid)

IT 59729-32-7P, Citalopram Hydrobromide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of pure citalopram by N-methylation of crude citalopram containing
desmethyl citalopram with formaldehyde and formic acid)
IT 50-00-0, Formaldehyde, reactions 544-92-3, Cuprous cyanide 6153-56-6, Oxalic acid dihydrate 10035-10-6, Hydrobromic acid, reactions 64169-39-7, 5-Bromo-1-(3-dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran 207559-01-1, Citalopram oxalate
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of pure citalopram by N-methylation of crude citalopram containing desmethyl citalopram with formaldehyde and formic acid)
IT 59729-33-8P, Citalopram
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation of pure citalopram by N-methylation of crude citalopram containing
desmethyl citalopram with formaldehyde and formic acid)
RN 59729-33-8 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



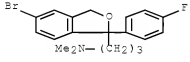
IT 59729-32-7P, Citalopram Hydrobromide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of pure citalopram by N-methylation of crude citalopram containing
desmethyl citalopram with formaldehyde and formic acid)
RN 59729-32-7 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



IT 64169-39-7, 5-Bromo-1-(3-dimethylaminopropyl)-1-(4-fluorophenyl)-

1,3-dihydroisobenzofuran
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of pure citalopram by N-methylation of crude citalopram containing desmethyl citalopram with formaldehyde and formic acid)

RN 64169-39-7 HCAPLUS
CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 22 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:777773 HCAPLUS Full-text
DOCUMENT NUMBER: 139:276808
TITLE: Transalification process for the preparation of purified citalopram hydrochloride or hydrobromide
INVENTOR(S): Hamied, Yusuf Khwaja; Kankan, Rajendra N.; Rao, Dharmaraj R.
PATENT ASSIGNEE(S): Cipla Ltd., India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080589	A1	20031002	WO 2003-GB1032	20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003212524	A1	20031008	AU 2003-212524	20030311
EP 1485367	A1	20041215	EP 2003-708344	20030311
EP 1485367	B1	20070801		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008603	A	20050209	BR 2003-8603	20030311
IN 2004MN00550	A	20060505	IN 2004-MN550	20041001
PRIORITY APPLN. INFO.:			GB 2002-6708 A	20020321
			WO 2003-GB1032 W	20030311

AB Purified citalopram hydrochloride or hydrobromide are made by purifying another different citalopram salt (e.g., citalopram besylate by

crystallization) and then converting the purified salt to the hydrochloride or hydrobromide.

IC ICM C07D307-87
ICS A61K031-343

CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 45, 48, 63

IT 606932-12-1P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(transalification process for the preparation of purified citalopram hydrochloride or hydrobromide)

IT 98-11-3, Benzenesulfonic acid, reactions 59729-33-8, Citalopram
RL: RCT (Reactant); RACT (Reactant or reagent)
(transalification process for the preparation of purified citalopram hydrochloride or hydrobromide)

IT 59729-32-7P, Citalopram hydrobromide 85118-27-0P, Citalopram hydrochloride
RL: SPN (Synthetic preparation); PREP (Preparation)
(transalification process for the preparation of purified citalopram hydrochloride or hydrobromide)

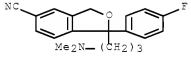
IT 606932-12-1P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(transalification process for the preparation of purified citalopram hydrochloride or hydrobromide)

RN 606932-12-1 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monobenzenesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8
CMF C20 H21 F N2 O

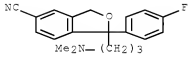


CM 2

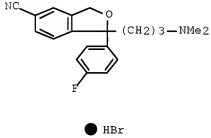
CRN 98-11-3
CMF C6 H6 O3 S

IT 59729-33-8, Citalopram

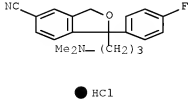
RL: RCT (Reactant); RACT (Reactant or reagent)
(transalification process for the preparation of purified citalopram hydrochloride or hydrobromide)
RN 59729-33-8 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



IT 59729-32-7P, Citalopram hydrobromide 85118-27-0P, Citalopram hydrochloride
RL: SPN (Synthetic preparation); PREP (Preparation)
(transalification process for the preparation of purified citalopram hydrochloride or hydrobromide)
RN 59729-32-7 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



RN 85118-27-0 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrochloride (1:1) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 23 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN

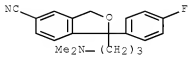
ACCESSION NUMBER: 2003:696884 HCAPLUS Full-text
DOCUMENT NUMBER: 139:230614
TITLE: Adsorption-washing-desorption process for the purification of citalopram
INVENTOR(S): Hamied, Yusuf Khwaja; Kankan, Rajendra N.; Rao, Dharmaraj R.
PATENT ASSIGNEE(S): Cipla Ltd., India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072564	A1	20030904	WO 2003-GB836	20030227
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
GB 2386119	A	20030910	GB 2002-4682	20020227
AU 2003208456	A1	20030909	AU 2003-208456	20030227
EP 1478638	A1	20041124	EP 2003-706744	20030227
EP 1478638	B1	20060809		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008062	A	20041228	BR 2003-8062	20030227
PRIORITY APPLN. INFO.:			GB 2002-4682 A	20020227
			WO 2003-GB836 W	20030227

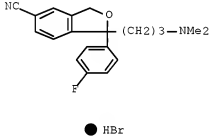
AB Crude citalopram base is purified by adsorption on a solid support (e.g., Celite), washing the support-adsorbed citalopram to selectively remove impurities with an aliphatic-aromatic hydrocarbon solvent mixture (e.g., hexane and toluene), and desorbing the purified base from the support by contact with a polar solvent (e.g., Et acetate). The purified citalopram is then salified with an acid (e.g., aqueous hydrogen bromide) to produce a pharmaceutically acceptable citalopram salt (e.g., citalopram hydrobromide).

IC ICM C07D307-87
ICS A61K031-343; A61P025-24
CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 45, 63
IT 59729-33-8P, Citalopram
RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); RCT (Reactant); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(adsorption-washing-desorption process for the purification of citalopram)
IT 59729-32-7P, Citalopram hydrobromide
RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(salification of citalopram base with acids in the preparation of pharmaceutically acceptable citalopram salts)
IT 59729-33-8P, Citalopram

RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); RCT (Reactant); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(adsorption-washing-desorption process for the purification of citalopram)
RN 59729-33-8 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



IT 59729-32-7P, Citalopram hydrobromide
RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(salification of citalopram base with acids in the preparation of pharmaceutically acceptable citalopram salts)
RN 59729-32-7 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 24 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:696883 HCAPLUS Full-text
DOCUMENT NUMBER: 139:214318
TITLE: Chromatographic process for the purification of amorphous citalopram and the preparation of citalopram salts
INVENTOR(S): Hamied, Yusuf Khwaja; Kankan, Rajendra N.; Rao, Dharmaraj R.
PATENT ASSIGNEE(S): Cipla Ltd., India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072562	A1	20030904	WO 2003-GB810	20030226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
GB 2386118	A	20030910	GB 2002-4680	20020227
AU 2003207348	A1	20030909	AU 2003-207348	20030226
EP 1478636	A1	20041124	EP 2003-704820	20030226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008060	A	20041228	BR 2003-8060	20030226
IN 2004MN00542	A	20050520	IN 2004-MN542	20040930
PRIORITY APPLN. INFO.:			GB 2002-4680 A	20020227
			WO 2003-GB810 W	20030226

AB Citalopram base is purified and isolated by chromatog. techniques and then subjected to spray drying and salification with aqueous HBr for the preparation of citalopram hydrobromide.

IC ICM C07D307-87
ICS A61K031-343; A61P025-24

CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 45, 48

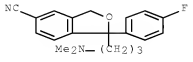
IT 59729-33-8P, Citalopram
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PUR (Purification or recovery); PYP (Physical process); RCT (Reactant); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(chromatog. process for the purification of amorphous citalopram and the preparation of citalopram salts)

IT 59729-32-7P, Citalopram hydrobromide
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(chromatog. process for the purification of amorphous citalopram and the preparation of citalopram salts)

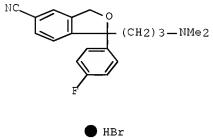
IT 59729-33-8P, Citalopram
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PUR (Purification or recovery); PYP (Physical process); RCT (Reactant); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(chromatog. process for the purification of amorphous citalopram and the preparation of citalopram salts)

RN 59729-33-8 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



IT 59729-32-7P, Citalopram hydrobromide
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(chromatog. process for the purification of amorphous citalopram and the preparation of citalopram salts)
RN 59729-32-7 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 25 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:590880 HCAPLUS Full-text
DOCUMENT NUMBER: 139:133459
TITLE: Cyanation process for the preparation of citalopram and its extractive purification
INVENTOR(S): Coppi, Laura; Gasanz Guillen, Yolanda; Campon Pardo, Julio
PATENT ASSIGNEE(S): Esteve Quimica, S.A., Spain
SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003144534	A1	20030731	US 2003-351289	20030124
US 6635773	B2	20031021		
ES 2194597	A1	20031116	ES 2002-167	20020125
ES 2194597	B2	20040801		
CA 2474323	A1	20030731	CA 2003-2474323	20030124
WO 2003062218	A1	20030731	WO 2003-ES37	20030124

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,

BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1479673	A1	20041124	EP 2003-706634		20030124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005522419	T	20050728	JP 2003-562097		20030124
CN 1688565	A	20051026	CN 2003-802625		20030124
ZA 2004005441	A	20050708	ZA 2004-5441		20040708
IN 2004KN00960	A	20060505	IN 2004-KN960		20040708
MX 2004PA07156	A	20041029	MX 2004-PA7156		20040723
NO 2004003568	A	20040825	NO 2004-3568		20040825
PRIORITY APPLN. INFO.:			ES 2002-167	A	20020125
			WO 2003-ES37	W	20030124

AB Crude citalopram was prepared the cyanation of 1-[3-(dimethylamine)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-bromoisobenzofuran with copper cyanide and purified citalopram or one of its salts (e.g., citalopram hydrobromide) was obtained by the extractive purification of citalopram by selective extns. of citalopram or it salts of its impurities with organic solvents (e.g., toluene and heptane) and water under specific conditions of pH and temperature

IC ICM C07D307-87

INCL 549467000

CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 45, 48

IT 59729-33-8P, Citalopram
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(cyanation process for the preparation of citalopram and its extractive purification)

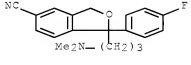
IT 544-92-3, Copper cyanide 64169-39-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyanation process for the preparation of citalopram and its extractive purification)

IT 59729-32-7P, Citalopram hydrobromide
RL: SPN (Synthetic preparation); PREP (Preparation)
(cyanation process for the preparation of citalopram and its extractive purification)

IT 59729-33-8P, Citalopram
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(cyanation process for the preparation of citalopram and its extractive purification)

RN 59729-33-8 HCAPLUS

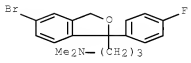
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



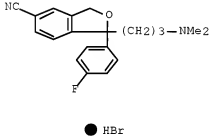
IT 64169-39-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyanation process for the preparation of citalopram and its extractive purification)

RN 64169-39-7 HCAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (CA INDEX NAME)



IT 59729-32-7P, Citalopram hydrobromide
RL: SPN (Synthetic preparation); PREP (Preparation)
(cyanation process for the preparation of citalopram and its extractive purification)
RN 59729-32-7 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



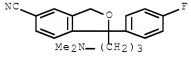
L38 ANSWER 26 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:559857 HCAPLUS Full-text
DOCUMENT NUMBER: 139:101019
TITLE: Preparation of high-purity citalopram and its acid salts from 1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile and 3-(dimethylamino)propyl chloride
INVENTOR(S): Arai, Nobuhiro; Ikemoto, Tetsuya; Iki, Masami
PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003206284	A	20030722	JP 2001-401695	20011228
PRIORITY APPLN. INFO.:			JP 2001-401695	20011228

AB Citalopram (I), useful as an antidepressant (no data), or its salts are prepared by treatment of the carbonitrile (II) with the chloride (III) in the presence of condensing agents and treatment of the reaction mixture with NaHSO3 in the presence of water to increase water solubility of byproducts and remove them. Alternatively, the reaction mixture is heated at ≥65° (after

salt formation). Thus, II was condensed with III in the presence of NaH and aqueous NaHSO3 solution added to give 97% I with purity 92.88%.

IC ICM C07D307-87
ICS A61K031-343; A61P025-24
CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
IT 59729-33-8P, Citalopram
RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(purification of high-purity citalopram as antidepressant)
IT 59729-32-7P, Citalopram hydrobromide
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(purification of high-purity citalopram as antidepressant)
IT 59729-33-8P, Citalopram
RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(purification of high-purity citalopram as antidepressant)
RN 59729-33-8 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



IT 59729-32-7P, Citalopram hydrobromide
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(purification of high-purity citalopram as antidepressant)
RN 59729-32-7 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)

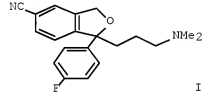
● HBr

L38 ANSWER 27 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:172971 HCAPLUS Full-text
DOCUMENT NUMBER: 138:221462

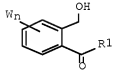
TITLE: Improved process for the manufacture of citalopram hydrobromide from 5-bromophthalide
PATENT ASSIGNEE(S): Sekhsaria Chemicals Ltd., India
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1288211	A1	20030305	EP 2002-255750	20020819
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRIORITY APPLN. INFO.:			US 2001-315391P	P 20010828
OTHER SOURCE(S):	CASREACT 138:221462; MARPAT 138:221462			

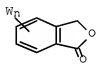
GI



I



II



III

AB A process for the preparation of 1-(4'-fluorophenyl)-1-(3-dimethylamino-propyl)- 5-phthalanecarbonitrile (I), or a pharmaceutically acceptable salt thereof, comprising performing two successive Grignard reactions on 5-bromophthalide, wherein the 5-bromophthalide is reacted with the first Grignard reagent in the presence of a Lewis acid, so reducing byproduct formation and improving yields. Also claimed is a process for the preparation of aryl ketone II [R1 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, aralkyl, optionally containing one heteroatom; W = haloge, CN, OH, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, aralkyl; n = 0 - 4] which comprises the step of reacting a phthalide III with a Grignard reagent, R1MgY (Y = halogen) and is charactetrized in that the phthalide is reacted with a Lewis acid to form an adduct prior to reaction with the Grignard reagent. Thus,.

IC ICM C07D307-87
CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
IT 59729-32-7P, Citalopram hydrobromide 207559-01-1P, Citalopram oxalate 500733-84-6P, Citalopram acetate

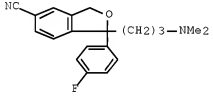
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(improved process for the manufacture of citalopram hydrobromide from 5-bromophthalide)

IT 59729-33-8P, Citalopram
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(improved process for the manufacture of citalopram hydrobromide from 5-bromophthalide)

IT 64169-39-7P, 1-(4-Fluorophenyl)-1-(3-dimethylamino-propyl)-5-bromophthalane
RL: PCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyanation of; improved process for the manufacture of citalopram
hydrobromide from 5-bromophthalide)

IT 59729-32-7P, Citalopram hydrobromide 207559-01-1P, Citalopram oxalate 500733-84-6P, Citalopram acetate
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(improved process for the manufacture of citalopram hydrobromide from 5-bromophthalide)

RN 59729-32-7 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)

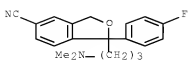


● HBr

RN 207559-01-1 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1) (CA INDEX NAME)

CM 1

CRN 59729-33-8
CMF C20 H21 F N2 O



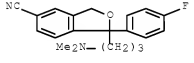
CM 2

CRN 144-62-7
CMF C2 H2 O4

RN 500733-84-6 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monoacetate (9CI) (CA INDEX NAME)

CM 1

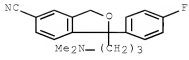
CRN 59729-33-8
CMF C20 H21 F N2 O



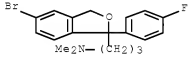
CM 2

CRN 64-19-7
CMF C2 H4 O2

IT 59729-33-8P, Citalopram
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(improved process for the manufacture of citalopram hydrobromide from 5-bromophthalide)
RN 59729-33-8 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



IT 64169-39-7P, 1-(4-Fluorophenyl)-1-(3-dimethylamino-propyl)-5-bromophthalane
RL: PCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyanation of; improved process for the manufacture of citalopram
hydrobromide from 5-bromophthalide)
RN 64169-39-7 HCAPLUS
CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 28 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:58074 HCAPLUS Full-text
DOCUMENT NUMBER: 138:122548
TITLE: Method for the preparation of escitalopram via chromatographic resolution of citalopram or its intermediates using carbohydrate-based chiral stationary phases
INVENTOR(S): Bech Sommer, Michael; Nielsen, Ole; Petersen, Hans; Ahmadian, Haleh; Pedersen, Henrik; Brosen, Peter; Geiser, Fiona; Lee, James; Cox, Geoffey; Dapremont, Olivier; Suteu, Christina; Assenza, Sebastian P.; Hariharan, Shankar; Nair, Usha
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003006449	A1	20030123	WO 2002-DK491	20020712
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,				

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

TW 268926	B	20061221	TW 2002-91115430	20020711	
CA 2451124	A1	20030123	CA 2002-2451124	20020712	
AU 2002354525	A1	20030129	AU 2002-354525	20020712	
EP 1409472	A1	20040421	EP 2002-750836	20020712	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
BR 2002010817	A	20040622	BR 2002-10817	20020712	
CN 1527825	A	20040908	CN 2002-813998	20020712	
HU 2004001451	A2	20041129	HU 2004-1451	20020712	
HU 2004001451	A3	20070529			
JP 2004538276	T	20041224	JP 2003-512221	20020712	
ZA 2003009471	A	20041206	ZA 2003-9471	20031205	
MX 2004PA00205	A	20040318	MX 2004-PA205	20040108	
BG 108572	A	20050331	BG 2004-108572	20040209	
IN 2004CN00293	A	20051209	IN 2004-CN293	20040212	
US 2005065207	A1	20050324	US 2004-483824	20040930	
PRIORITY APPLN. INFO.:			DK 2001-1101	A	20010713
			DK 2001-1851	A	20011211
			DK 2001-1852	A	20011211
			WO 2002-DK491	W	20020712

OTHER SOURCE(S): CASREACT 138:122548
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A novel method is provided for the manufacture of the antidepressant escitalopram, i.e., (S)-I. The method comprises chromatog. separation of the enantiomers of either (1) citalopram, i.e., (±)-I, or (2) an intermediate in its production, using a chiral stationary phase such as Chiralpak AD or Chiralcel OD. Novel chiral intermediates for the synthesis of escitalopram, made by said method, are also provided. For example, the intermediate nitrile diol (±)-II was resolved using Chiralpak AD stationary phase on a Novasep Licosep 10-50 simulated moving bed chromatograph with MeCN mobile phase at 30°, to give both enantiomers of II with purity exceeding 99% ee. Similarly resolved in 96-99% yield and >99% ee were bromide diol (±)-III and bromophthalane (±)-IV, using Chiralpak AD and Chiralcel OD, resp. Resolution of (±)-IV was performed on a 500-g scale using 98:2 isohexane/isopropanol (vol/vol), and also on a smaller scale using supercrit. CO2 with MeOH/Et2NH/CF3CO2H modifier. The obtained bromide (S)-(+)-IV underwent cyanation by Zn(CN)2 and Pd(PPh3)4 according to the method of WO 00/13648, giving escitalopram in 80% yield and 99.6% ee.

IC ICM C07D307-87
ICS C07B057-00

CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 45

IT 488148-12-5P, (S)-1-[4-Bromo-2-(hydroxymethyl)phenyl]-4-(dimethylamino)-1-(4-fluorophenyl)butan-1-ol 488148-14-7P, (S)-(+)-1-(4-Fluorophenyl)-1-[3-(dimethylamino)propyl]-5-bromophthalane 488148-15-8P, (S)-1-(4-Fluorophenyl)-1-[3-(dimethylamino)propyl]-5-[[(trifluoromethyl)sulfonyl]oxy]phthalane 488148-16-9P, (S)-1-(4-Fluorophenyl)-1-[3-(dimethylamino)propyl]-5-[[(perfluoroethyl)sulfonyl]oxy]phthalane 488148-17-0P,

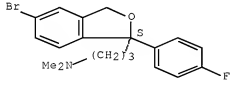
(S)-1-(4-Fluorophenyl)-1-[3-(dimethylamino)propyl]-5-[[(perfluoropropyl)sulfonyl]oxy]phthalane 488148-18-1P,
(S)-1-(4-Fluorophenyl)-1-[3-(dimethylamino)propyl]-5-[[(perfluorobutyl)sulfonyl]oxy]phthalane 488148-19-2P,
(S)-1-(4-Fluorophenyl)-1-[3-(dimethylamino)propyl]-5-[[(perfluoropentyl)sulfonyl]oxy]phthalane 488148-20-5P,
(S)-1-(4-Fluorophenyl)-1-[3-(dimethylamino)propyl]-5-[[(perfluorohexyl)sulfonyl]oxy]phthalane 488148-21-6P,
(S)-1-(4-Fluorophenyl)-1-[3-(dimethylamino)propyl]-5-[[(perfluoroheptyl)sulfonyl]oxy]phthalane 488148-22-7P,
(S)-1-(4-Fluorophenyl)-1-[3-(dimethylamino)propyl]-5-[[(perfluorooctyl)sulfonyl]oxy]phthalane 488148-23-8P,
(S)-1-(4-Fluorophenyl)-1-[3-(dimethylamino)propyl]-5-[[(perfluorononyl)sulfonyl]oxy]phthalane 488787-59-3P,
(S)-4-[4-(Dimethylamino)-1-(4-fluorophenyl)-1-hydroxy-1-butyl]-3-(hydroxymethyl)benzonitrile
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(intermediate enantiomer; preparation of escitalopram via chromatog. resolution
of citalopram or intermediates using carbohydrate-based chiral stationary phases)

IT 128196-01-0P, Escitalopram
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation of escitalopram via chromatog. resolution of citalopram or intermediates using carbohydrate-based chiral stationary phases)

IT 488148-14-7P, (S)-(+)-1-(4-Fluorophenyl)-1-[3-(dimethylamino)propyl]-5-bromophthalane 488787-59-3P, (S)-4-[4-(Dimethylamino)-1-(4-fluorophenyl)-1-hydroxy-1-butyl]-3-(hydroxymethyl)benzonitrile
RL: PUR (Purification or recovery); PCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(intermediate enantiomer; preparation of escitalopram via chromatog. resolution
of citalopram or intermediates using carbohydrate-based chiral stationary phases)

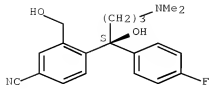
RN 488148-14-7 HCAPLUS
CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



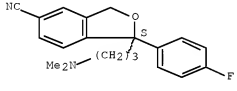
RN 488787-59-3 HCAPLUS
CN Benzonitrile, 4-[(1S)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 128196-01-0P, Escitalopram
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation of escitalopram via chromatog. resolution of citalopram or intermediates using carbohydrate-based chiral stationary phases)
RN 128196-01-0 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 29 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:32670 HCAPLUS Full-text
DOCUMENT NUMBER: 138:55856
TITLE: Process for the preparation of highly pure salts of citalopram
INVENTOR(S): Satyanarayana, Chava; Venkata, Ramana Rao Chunchu; Jyothi, Basu Abbineni; Hari, Babu Bobepudi
PATENT ASSIGNEE(S): Matrix Laboratories Limited, India
SOURCE: Brit. UK Pat. Appl., 18 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2375763	A	20021127	GB 2002-10225	20020503
GB 2375763	B	20030924		
CA 2444940	A1	20030904	CA 2002-2444940	20020418
WO 2003072565	A1	20030904	WO 2002-IB3832	20020418
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU	2002367728	A1	20030909	AU 2002-367728		20020418
BR	2002009194	A	20040608	BR 2002-9194		20020418
CN	1509279	A	20040630	CN 2002-809801		20020418
EP	1478635	A1	20041124	EP 2002-806883		20020418
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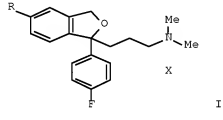
JP	2005518445	T	20050623	JP 2003-571271		20020418
NZ	529070	A	20060224	NZ 2002-529070		20020418
GB	2387596	A	20031022	GB 2003-15853		20020503
GB	2387596	B	20040211			
GB	2387844	A	20031029	GB 2003-15852		20020503
GB	2387844	B	20050511			
IN	2003DN01674	A	20070831	IN 2003-DN1674		20031015
ZA	2003008115	A	20040705	ZA 2003-8115		20031017
MX	2003PA09695	A	20050307	MX 2003-PA9695		20031023

PRIORITY APPLN. INFO.:

GB 2002-4607	A	20020227
WO 2002-IB3832	W	20020418
GB 2002-10225	A	20020503

GI



I

AB A process for preparing highly pure salts of citalopram, such as I (R = CN; X = oxalate, hydrobromide, hydrochloride), for pharmaceutical compns. was described. Thus, citalopram contaminated with up to 5.0% of desmethyl citalopram was added to acetone and stirred for 15 min at 40° followed by addn of oxalic acid to form citalopram oxalate in 85% yield with desmethyl citalopram content <0.1%.

IC ICM C07D307-87

CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 63

IT 59729-33-8P, Citalopram 207559-01-1P, Citalopram oxalate
RL: IMF (Industrial manufacture); PUR (Purification or recovery)
; RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(process for the preparation of highly pure salts of citalopram)

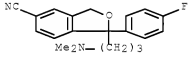
IT 65118-27-0P, Citalopram hydrochloride
RL: IMF (Industrial manufacture); PUR (Purification or recovery)
; SPN (Synthetic preparation); PREP (Preparation)

(process for the preparation of highly pure salts of citalopram)

IT 59729-32-7P, Citalopram hydrobromide
RL: IMF (Industrial manufacture); PUR (Purification or recovery)
; SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for the preparation of highly pure salts of citalopram)

IT 59729-33-8P, Citalopram 207559-01-1P, Citalopram oxalate
RL: IMF (Industrial manufacture); PUR (Purification or recovery)
; RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(process for the preparation of highly pure salts of citalopram)

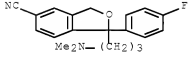
RN 59729-33-8 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



RN 207559-01-1 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1) (CA INDEX NAME)

CM 1

CRN 59729-33-8
CMF C20 H21 F N2 O

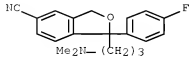


CM 2

CRN 144-62-7
CMF C2 H2 O4

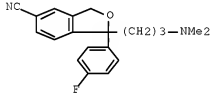
IT 85118-27-0P, Citalopram hydrochloride
RL: IMF (Industrial manufacture); PUR (Purification or recovery)
; SPN (Synthetic preparation); PREP (Preparation)

(process for the preparation of highly pure salts of citalopram)
RN 85118-27-0 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

IT 59729-32-7P, Citalopram hydrobromide
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for the preparation of highly pure salts of citalopram)
RN 59729-32-7 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



● HBr

L38 ANSWER 30 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:558778 HCAPLUS Full-text
DOCUMENT NUMBER: 135:192383
TITLE: Reduction of extraction times in liquid-phase microextraction
AUTHOR(S): Gronhaug Halvorsen, T.; Pedersen-Bjergaard, S.; Rasmussen, K. E.
CORPORATE SOURCE: School of Pharmacy, University of Oslo, Oslo, 0316, Norway
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (2001), 760(2), 219-226
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recently, the authors introduced a simple and inexpensive disposable device for liquid-phase microextn. (LPME) based on porous polypropylene hollow fibers. In the present paper, extraction times were significantly reduced by

an increase in the surface of the hollow fibers. The model compds. methamphetamine and citalopram, were extracted from 2.5 mL of urine, plasma, and whole blood after dilution with water and alkalization with 125 µL of 2M NaOH though a porous polypropylene hollow fiber impregnated with hexyl ether and into an aqueous acceptor phase consisting of 0.1M HCl. Two com. available hollow fibers, which differed in surface area, wall thickness and internal diameter, were compared. An increase in the contact area of the hollow fiber with the sample solution by a factor of approx. two resulted in reduction in equilibrium times by approx. the same factor. Thus, the model compds. were extracted to equilibrium within 15 min from both urine and plasma, and within 30 min from whole blood. For the first time LPME was utilized to extract drugs from whole blood, and the exts. were comparable with plasma both with regard to sample clean-up and extraction recoveries. Extraction recoveries for methamphetamine and citalopram varied from 60 to 100% using the two fibers and the different matrixes.

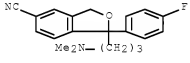
CC 9-9 (Biochemical Methods)

IT 537-46-2P, Methamphetamine 59729-33-8P, Citalopram
RL: PUR (Purification or recovery); PREP (Preparation)
(reduction of extraction times in liquid-phase microextn.)

IT 59729-33-8P, Citalopram
RL: PUF (Purification or recovery); PREP (Preparation)
(reduction of extraction times in liquid-phase microextn.)

RN 59729-33-8 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 31 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:489362 HCAPLUS Full-text

DOCUMENT NUMBER: 135:61225

TITLE: Process for the preparation of high-purity citalopram by cyanidation with purification via thin-film distillation

INVENTOR(S): Castellin, Andrea; Volpe, Giulio; Sbrogio, Federico

PATENT ASSIGNEE(S): H. Lundbeck A/s, Den.

SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047877	A2	20010705	WO 2001-DK148	20010307
WO 2001047877	A3	20001227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,

HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA	2359810	A1	20010705	CA 2001-2359810	20010307
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AU	200139202	A	20010709	AU 2001-39202	20010307
AU	2001100399	A4	20011101	AU 2001-100399	20010307
AU	2001100399	B4	20020321		
EP	1181272	A2	20020227	EP 2001-913727	20010307
EP	1181272	B1	20020828		

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BR	2001006271	A	20020521	BR 2001-6271	20010307
TR	200200018	T1	20020621	TR 2002-18	20010307
AT	222899	T	20020915	AT 2001-913727	20010307
PT	1181272	T	20030131	PT 2001-913727	20010307
ES	2181663	T3	20030301	ES 2001-1913727	20010307
JP	2003519121	T	20030617	JP 2001-549350	20010307
SK	284418	B6	20050401	SK 2001-1847	20010307
NL	1017534	C1	20010426	NL 2001-1017534	20010308
DK	2001000386	A	20020629	DK 2001-386	20010308
IN	193426	A1	20040717	IN 2001-MA215	20010309
GB	2356199	A	20010516	GB 2001-5981	20010312
GB	2356199	B	20011003		
CZ	293140	B6	20040218	CZ 2001-891	20010312
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NO	313047	B1	20020805		
GR	2001100131	A	20021009	GR 2001-100131	20010316
DE	10112828	C1	20021121	DE 2001-10112828	20010316
DE	10164725	A1	20030206	DE 2001-10164725	20010316
DE	10164725	B4	20040826		
CH	691536	A5	20010815	CH 2001-546	20010322
BE	1013417	A6	20011204	BE 2001-189	20010322
FR	2818977	A1	20020705	FR 2001-4025	20010326
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NL	1018410	C1	20011113	NL 2001-1018410	20010628
HU	2001002818	A2	20011228	HU 2001-2818	20010705
HU	2001002818	A3	20030728		
BE	1013316	A6	20011106	BE 2001-466	20010709
GB	2361697	A	20011031	GB 2001-17095	20010713
IN	193611	A1	20040724	IN 2001-MA580	20010713
CH	691999	A5	20010726	CH 2001-1412	20010726
ES	2170733	A1	20020801	ES 2001-1763	20010727
ES	2170733	B1	20031216		
AU	750006	B1	20020711	AU 2001-65478	20010827
SE	2001003044	A	20020629	SE 2001-3044	20010914
ZA	2001010133	A	20030113	ZA 2001-10133	20011210
BG	106219	A	20020830	BG 2001-106219	20011213
MX	2001PA13336	A	20020709	MX 2001-PA13336	20011219
US	2002087012	A1	20020704	US 2001-35005	20011220
US	6855834	B2	20050215		
NZ	516299	A	20021220	NZ 2001-516299	20011220
HR	2002000005	A1	20030430	HR 2002-5	20020104
US	2003178295	A1	20030925	US 2003-361800	20030210

PRIORITY APPLN. INFO.: DK 2000-1943 A 20001228

	WO 2001-DK148	W	20010307
	NL 2001-1017534	A	20010308
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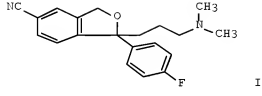
	US 2001-35005	A1	20011220

OTHER SOURCE(S): CASREACT 135:61225; MARPAT 135:61225

GI



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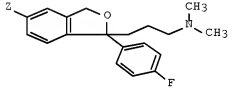


II

AB High-purity citalopram (I) is prepared on an industrial scale by: subjecting a citalopram precursor [II; Z = iodo, bromo, chloro, CF3(CF2)nSO2O; n = 0-8] (e.g., Z = Br) to a cyanide exchange reaction in which the group Z is exchanged with cyanide by reaction with a cyanide source (e.g., CuCN) in a solvent (e.g., sulfolane); the crude citalopram product is optionally subjected to some initial purification and the crude citalopram base is subsequently subjected to a thin- or falling-film distillation process.

IC ICM C07D

CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 45, 48

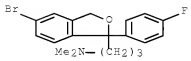
IT 544-92-3, Cuprous cyanide 557-21-1, Zinc cyanide 64169-39-7
64169-45-5 260066-78-2 260066-82-8 345658-19-7 345658-20-0
345658-21-1 345658-22-2 345658-23-3 345658-24-4 345658-25-5
345658-26-6
RL: PCT (Reactant); PACT (Reactant or reagent)
(in a process for the preparation of high-purity citalopram by cyanidation with purification via thin-film distillation)

IT 59729-33-8P, Citalopram
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PPEP (Preparation)
(process for the preparation of high-purity citalopram by cyanidation with purification via thin-film distillation)

IT 64169-39-7
RL: PCT (Reactant); PACT (Reactant or reagent)
(in a process for the preparation of high-purity citalopram by cyanidation with purification via thin-film distillation)

RN 64169-39-7 HCAPLUS

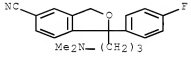
CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (CA INDEX NAME)



IT 59729-33-8P, Citalopram
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for the preparation of high-purity citalopram by cyanidation with purification via thin-film distillation)

RN 59729-33-8 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



L38 ANSWER 32 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:472398 HCAPLUS Full-text
DOCUMENT NUMBER: 135:61224
TITLE: Method for the preparation and purification of citalopram
INVENTOR(S): Villa, Marcos; Sbrogio, Federico; Dancer, Robert
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001045483	A2	20010628	WO 2001-DK147	20010307
WO 2001045483	A3	20011227		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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CA 2360303	A1	20010628	CA 2001-2360303		20010307
CA 2360303	C	20030812			
AU 2001100405	A4	20011101	AU 2001-100405		20010307
AU 2001100405	B4	20020321			
EP 1181713	A2	20020227	EP 2001-913726		20010307
EP 1181713	B1	20040929			
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TR 200201166	T1	20021021	TR 2002-1166		20010307
JP 2003517484	T	20030527	JP 2001-546230		20010307
JP 3798982	B2	20060719			
BR 200100672	A	20040615	BR 2001-672		20010307
EP 1462447	A2	20040929	EP 2004-4482		20010307
EP 1462447	A3	20041117			
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PT 1181713	T	20050228	PT 2001-913726		20010307
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ES 2228824	T3	20050416	ES 2001-1913726		20010307
DK 174018	B1	20020422	DK 2001-402		20010308
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GB 2359811	B	20030305			
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FR 2812877	B1	20030404			
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HU 2001002817	A2	20011228	HU 2001-2817		20010705
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ES 2170732	A1	20020801	ES 2001-1762		20010727
AU 744112	B1	20020214	AU 2001-65477		20010827
SE 2001003045	A	20020623	SE 2001-3045		20010914
SE 517623	C2	20020625			
BG 106203	A	20020830	BG 2001-106203		20011210
BG 65131	B1	20070330			
ZA 2001010179	A	20021211	ZA 2001-10179		20011211
MX 2001PA13151	A	20020812	MX 2001-PA13151		20011218
NZ 516298	A	20021220	NZ 2001-516298		20011220
HR 2002000004	A1	20030430	HR 2002-4		20020104
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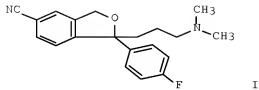
HK 1048812	A1	20070601	HK 2003-100966		20030210
PRIORITY APPLN. INFO.:			DK 2000-1929	A	20001222
			NL 2001-1017525	A	20001222
			EP 2001-913726	A3	20010307
			WO 2001-DK147	W	20010307
			GB 2001-5983	A3	20010312
			CH 2001-545	A	20010322
OTHER SOURCE(S):	CASREACT 135:61224; MARPAT 135:61224				

GI



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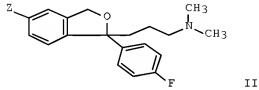


II

AB A process for the preparation and purification of citalopram (I) is presented in which a benzoisofuran derivative [II; Z = iodo, bromo, chloro, CF3(CF2)nSO2O; n = 0-8] is subjected to a cyanide-exchange reaction with a cyanide source (e.g., cuprous cyanide). The resultant crude citalopram is optionally subjected to some initial purification and subsequently treated with an amide or an amide-like group forming agent (e.g., acetic anhydride), the reaction mixture is then subjected to an acid/base wash and/or crystallization and recrystn. of citalopram in order to remove the amides formed from the crude citalopram mixture, and the resulting citalopram product is optionally further purified, worked up and isolated as the base or a pharmaceutically acceptable salt.

CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 45

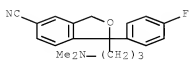
IT 59729-33-8P, Citalopram
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(method for the preparation and purification of citalopram)

IT 64169-39-7 64169-45-5 260066-78-2 260066-82-8 345658-19-7 345658-20-0 345658-21-1 345658-22-2 345658-23-3 345658-24-4 345658-25-5 345658-26-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(method for the preparation of citalopram by the cyanidation of)

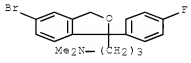
IT 59729-33-8P, Citalopram
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(method for the preparation and purification of citalopram)

RN 59729-33-8 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)

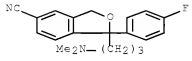


IT 64169-39-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(method for the preparation of citalopram by the cyanidation of)
RN 64169-39-7 HCAPLUS
CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (CA INDEX NAME)



L38 ANSWER 33 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:181925 HCAPLUS Full-text
DOCUMENT NUMBER: 135:70537
TITLE: On-line extraction using an alkyl-diol silica precolumn for racemic citalopram and its metabolites in plasma. Results compared with solid-phase extraction methodology
AUTHOR(S): Ohman, D.; Carlsson, B.; Norlander, B.
CORPORATE SOURCE: Faculty of Health Sciences, Department of Medicine and Care, Clinical Pharmacology, Linkoping University, Linkoping, S-581 85, Swed.
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (2001), 753(2), 365-373
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sample preparation is usually the most critical and time consuming step when using HPLC for drug anal. in biol. matrixes. Sample exts. have to be clean considering both chromatog. interferences and column maintenance. To meet some of these criteria a fully automated online extraction (OLE) anal. method was developed for the antidepressant drug citalopram and its two demethylated metabolites, using an RP-C4-ADS extraction column. A comparison between the new OLE method and an off-line solid-phase extraction method showed that the two methodologies were equal in anal. precision but that the OLE method was faster and therefore superior in sample capacity per day.
CC 1-1 (Pharmacology)
IT 59729-33-8P, Citalopram 62498-67-3P, Demethylcitalopram 62498-69-5P, Didemethylcitalopram
RL: ANT (Analyte); PUP (Purification or recovery); ANST (Analytical study); PREP (Preparation)
(online extraction using an alkyl-diol silica precolumn for racemic citalopram and its metabolites in plasma and comparison with solid-phase extraction methodol.)
IT 59729-33-8P, Citalopram
RL: ANT (Analyte); PUR (Purification or recovery); ANST (Analytical study); PREP (Preparation)
(online extraction using an alkyl-diol silica precolumn for racemic citalopram and its metabolites in plasma and comparison with solid-phase extraction methodol.)

RN 59729-33-8 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 34 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:607941 HCAPLUS Full-text
DOCUMENT NUMBER: 133:213148
TITLE: Crystalline base of citalopram
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: Ger. Gebrauchsmusterschrift, 17 pp.
CODEN: GGXXFR
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 20007303	U1	20000831	DE 2000-20007303	20000420
GB 2357762	A	20010704	GB 2001-5982	20000413
GB 2357762	B	20020130		
NL 1016435	C1	20001106	NL 2000-1016435	20001018
IT 2000MI2425	A1	20020509	IT 2000-MI2425	20001109
IT 1319645	B1	20031023		
US 2001031784	A1	20011018	US 2000-730490	20001205
IN 2001MA00091	A	20050304	IN 2001-MA91	20010201
HU 2001000531	A2	20020128	HU 2001-531	20010205
DK 173903	B1	20020211	DK 2001-183	20010205
HU 2004000868	A3	20070529	HU 2004-868	20010205
NO 2001000619	A	20010914	NO 2001-619	20010206
NO 312031	B1	20020304		
FI 2001000225	A	20010914	FI 2001-225	20010207
FI 109022	B1	20020515		
GR 1003796	B2	20020208	GR 2001-100074	20010212
DE 10108042	A1	20011018	DE 2001-10108042	20010220
DE 20121240	U1	20020808	DE 2001-20121240	20010220
DE 10164687	B4	20060427	DE 2001-10164687	20010220
NL 1017413	C1	20010913	NL 2001-1017413	20010221
FR 2806086	A1	20010914	FR 2001-2340	20010221
FR 2806086	B1	20030509		
CH 691477	A5	20010731	CH 2001-321	20010222
CH 691537	A5	20010815	CH 2001-580	20010222
AU 200137252	A	20010913	AU 2001-37252	20010228
AU 746664	B2	20020502		
CA 2360287	A1	20010920	CA 2001-2360287	20010228
CA 2360287	C	20030909		
CA 2411732	A1	20010920	CA 2001-2411732	20010228
WO 2001068627	A1	20010920	WO 2001-DK137	20010228

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

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BE	1013210	A3	20011002	BE 2001-136	20010228
EP	1169314	A1	20020109	EP 2001-909568	20010228
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EP	1227088	A1	20020731	EP 2002-9350	20010228
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AT	223396	T	20020915	AT 2001-909568	20010228
PT	1169314	T	20021129	PT 2001-909568	20010228
ES	2173054	T3	20021216	ES 2001-1909568	20010228
TR	200202185	T2	20021223	TR 2002-2185	20010228
BR	2001009373	A	20021224	BR 2001-9373	20010228
JP	2003527383	T	20030916	JP 2001-567719	20010228
AT	250050	T	20031015	AT 2002-9350	20010228
PT	1227088	T	20031231	PT 2002-9350	20010228
ES	2180471	T3	20040501	ES 2002-2009350	20010228
CN	1680350	A	20051012	CN 2005-10009160	20010228
SK	285528	B6	20070301	SK 2002-1313	20010228
CZ	292077	B6	20030716	CZ 2001-808	20010305
IN	193191	A1	20040710	IN 2001-MA209	20010308
ES	2159491	A1	20011001	ES 2001-548	20010309
ES	2159491	B1	20020501		
AU	2001100197	A4	20010920	AU 2001-100197	20010726
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SE	2001003046	A	20011114	SE 2001-3046	20010914
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NO	2002000356	A	20010914	NO 2002-356	20020123
NO	315851	B1	20031103		
SE	2002000730	A	20020829	SE 2002-730	20020312
SE	526022	C2	20050614		
ZA	2002007148	A	20030423	ZA 2002-7148	20020905
BG	107065	A	20030530	BG 2002-107065	20020905
MX	2002PA08793	A	20030212	MX 2002-PA8793	20020909
US	2003078442	A1	20030424	US 2002-245824	20020912
IN	2002MA00828	A	20050304	IN 2002-MA828	20021111
HK	1054750	A1	20070119	HK 2003-107120	20031002
US	2004132808	A1	20040708	US 2003-741553	20031219
US	2004167210	A1	20040826	US 2003-750049	20031230
US	2005165092	A1	20050728	US 2005-90336	20050324
US	2005165244	A1	20050728	US 2005-90337	20050324
US	2006229459	A1	20061012	US 2006-425308	20060620
US	2006247451	A1	20061102	US 2006-425321	20060620

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CA 2003-2360287	A3	20030113
US 2003-741553	B1	20031219
US 2003-750049	B1	20031230
US 2005-90336	A1	20050324
US 2005-90337	B1	20050324

AB Citalopram, a selective, centrally acting serotonin reuptake inhibitor useful as an antidepressant, is prepared in high purity from a crude salt or reaction mixture containing citalopram by dissolving the latter in a mixture of H2O and an organic solvent, adding a base, separating and evaporating the organic phase, and crystallization from an aprotic solvent. The free base may then be converted to a salt by reaction with the stoichiometric amount of an acid (e.g. HCl, HBr) in a water-miscible solvent (e.g. Me2CO, EtOH), concentration, and cooling, or by reaction with an excess of acid in Et2O, EtOAc, or CH2Cl2 for formulation as tablets, capsules, powders, syrups, or solns. for injection.

IC C07D307-87

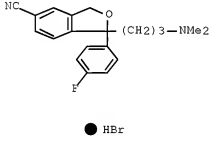
CC 63-6 (Pharmaceuticals)

IT 59729-32-7P, Citalopram hydrobromide 59729-33-8P, Citalopram 85118-27-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystalline base of citalopram)

IT 59729-32-7P, Citalopram hydrobromide 59729-33-8P, Citalopram 85118-27-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystalline base of citalopram)

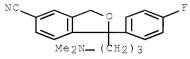
RN 59729-32-7 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



RN 59729-33-8 HCAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



RN 85118-27-0 HCAPLUS
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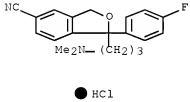
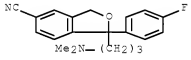


L38 ANSWER 35 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:154442 HCAPLUS Full-text
DOCUMENT NUMBER: 124:228035
TITLE: The serotonin transporter from human brain: purification and partial characterization
AUTHOR(S): Rotondo, A.; Giannaccini, G.; Betti, L.; Chiellini, G.; Marazziti, D.; Martin, C.; Lucacchini, A.; Cassano, G. B.
CORPORATE SOURCE: Inst. Psychiatry, Univ. Pisa, Pisa, 56100, Italy
SOURCE: Neurochemistry International (1996), 28(3), 299-307
CODEN: NEUIDS; ISSN: 0197-0186
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The serotonin (5-HT) transporter from human striatum was solubilized by digitonin and purified by affinity chromatog. The native protein-detergent complex had a mol. mass of 205 kDa, as estimated by gel-exclusion chromatog. of the eluates obtained from affinity chromatog. The purified 5-HT transporter migrated as a single band of 67 kDa in SDS-PAGE. To clarify the spatial relationships between the binding sites of the tricyclic antidepressants, as [3H]-imipramine, and of the selective serotonin reuptake inhibitors, such as [3H]-paroxetine, on the 5-HT transporter, both radioligands were used to label it in the purification steps. [3H]-paroxetine bound with the same affinity to a single high-affinity site on both membrane and purified prepns. [3H]-imipramine labeled a high- and a low-affinity site on parent membranes, whereas it bound to a single high-affinity site on the purified extract Tricyclic antidepressants, selective serotonin reuptake inhibitors and 5-HT itself displaced [3H]-paroxetine 5-HT transporter in a monophasic fashion with Hill coeffs. close to unity. Furthermore, both [3H]-paroxetine and [3H]-imipramine displayed a similar maximum binding capacity on an identical protein of 205 kDa. The results suggest overlapping binding sites for tricyclic antidepressants, selective serotonin reuptake inhibitors and 5-HT on the 5-HT transporter.

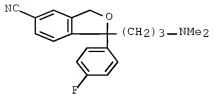
CC 13-6 (Mammalian Biochemistry)

Section cross-reference(s): 2
IT 50-47-5, Desipramine 50-49-7, Imipramine 50-67-9, 5-HT, biological studies 54910-89-3, Fluoxetine 59729-33-8, Citalopram 61869-08-7, Paroxetine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(purification and partial characterization of the serotonin transporter from human brain)
IT 59729-33-8, Citalopram
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(purification and partial characterization of the serotonin transporter from human brain)
RN 59729-33-8 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



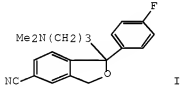
L38 ANSWER 36 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:225124 HCAPLUS Full-text
DOCUMENT NUMBER: 114:225124
TITLE: Approaches to the purification of the 5-hydroxytryptamine reuptake system from human blood platelets
AUTHOR(S): Biessen, Eric A. L.; Horn, Alan S.; Robillard, George T.
CORPORATE SOURCE: Inst. BIOSON, Univ. Groningen, Groningen, 9747 AG, Neth.
SOURCE: Biochemical Society Transactions (1991), 19(1), 103-11
CODEN: BCSTB5; ISSN: 0300-5127
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Physiol. pathway, mechanism and structure of Na+-dependent serotonergic reuptake, coupling between carrier and regulatory site, and platelets as a model system for neuronal reuptake are described. Development and application of affinity chromatog. resins for purification of the 5-HT-reuptake system is discussed. A series of resins consisting of immobilized citalopram, imipramine, and serotonin derivative were synthesized and tested for binding of 5-HT reuptake system.
CC 9-15 (Biochemical Methods)
Section cross-reference(s): 2
IT 50-47-5D, Desipramine, resins containing 50-67-9D, resins containing, biological studies 796-28-1D, 10-Hydroxyimipramine, resins containing 95945-60-1D, resins containing 133574-26-2D, resins containing 133761-84-9D, resins containing
RL: ANST (Analytical study)
(for 5-HT reuptake system purification from human blood platelets)
IT 133574-26-2D, resins containing
RL: BIOL (Biological study)
(for 5-HT reuptake system purification from human blood platelets)

RN 133574-26-2 HCAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, mono(methylamino) deriv. (9CI) (CA INDEX NAME)



D1—CH_2—NH_2

L38 ANSWER 37 OF 37 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1982:96989 HCAPLUS Full-text
DOCUMENT NUMBER: 96:96989
ORIGINAL REFERENCE NO.: 96:15721a,15724a
TITLE: Determination of the antidepressant agent citalopram and metabolites in plasma by liquid chromatography with fluorescence detection
AUTHOR(S): Oeyehaug, Ellen; Oestensen, Eilif Terje; Salvesen, Bjarne
CORPORATE SOURCE: Agder Coll., Kristiansand, 4600, Norway
SOURCE: Journal of Chromatography (1982), 227(1), 129-35
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A high-performance liquid chromatog. method is described for the determination of citalopram (I) [59729-33-8] (the methylamino [62498-67-3] and amino [62498-69-5] derivs.) and its two main metabolites. The compds. were extracted from alkaline plasma with di-Et ether. The combined ether layers were evaporated after addition of 50 μL of 0.1 N HCl. The residual exts. were purified with di-Et ether and 20 μL were injected into a Spherisorb ODS 5-μm column with MeCN-0.6% phosphate buffer pH 3 (55:45, volume/volume) as the mobile phase. Using a fluorescence detector, the detection limits are 1 ng/mL of plasma for citalopram and the methylamino metabolite and 0.5 ng/mL for the amino metabolite.
CC 1-1 (Pharmacology)

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=> d his nofil

     (FILE 'HOME' ENTERED AT 09:53:29 ON 28 DEC 2007)

     FILE 'CAPLUS' ENTERED AT 09:53:40 ON 28 DEC 2007
                E US2006-565736/APPS
L1            1 SEA ABB=ON  PLU=ON  US2006-565736/AP
                SEL RN

     FILE 'REGISTRY' ENTERED AT 10:01:59 ON 28 DEC 2007
L2           19 SEA ABB=ON  PLU=ON  (103146-25-4/BI OR 108-88-3/BI OR 110-17-8/
                BI OR 110-54-3/BI OR 124-63-0/BI OR 128196-01-0/BI OR 1310-58-3
                /BI OR 1310-73-2/BI OR 139-33-3/BI OR 141-78-6/BI OR 144-62-7/B
                I OR 488787-59-3/BI OR 59729-32-7/BI OR 59729-33-8/BI OR
                60-00-4/BI OR 64169-39-7/BI OR 75-09-2/BI OR 77-92-9/BI OR
                87-69-4/BI)

     FILE 'CAPLUS' ENTERED AT 10:02:22 ON 28 DEC 2007
L3            1 SEA ABB=ON  PLU=ON  L1 AND L2
                D IALL HITSTR

     FILE 'REGISTRY' ENTERED AT 10:04:14 ON 28 DEC 2007
                E CITALOPRAM/CN
L4            1 SEA ABB=ON  PLU=ON  CITALOPRAM/CN
                D

     FILE 'REGISTRY' ENTERED AT 10:04:34 ON 28 DEC 2007
L5              STR 59729-33-8
L6           63 SEA FAM FUL L5

     FILE 'CAPLUS' ENTERED AT 10:04:44 ON 28 DEC 2007
L7           29 SEA ABB=ON  PLU=ON  L6(L)PUR+NT/RL
L8            1 SEA ABB=ON  PLU=ON  L7 AND L1
L9          143 SEA ABB=ON  PLU=ON  L6(L)PREP+NT/RL
L10          22 SEA ABB=ON  PLU=ON  L6(L)(PURIF? OR RECOVER?)
L11          42 SEA ABB=ON  PLU=ON  L7 OR L10
L12          15 SEA ABB=ON  PLU=ON  L6(L)PURIF?
L13          35 SEA ABB=ON  PLU=ON  L12 OR L7

     FILE 'REGISTRY' ENTERED AT 10:09:02 ON 28 DEC 2007
L14           1 SEA ABB=ON  PLU=ON  103146-25-4

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L15             STR 103146-25-4
L16          25 SEA FAM FUL L15
L17           0 SEA ABB=ON  PLU=ON  PHTHAL?/CNS AND L2
                E PHTHALANE/CN
L18           2 SEA ABB=ON  PLU=ON  L2 AND BR/ELS
                D SCA

     FILE 'REGISTRY' ENTERED AT 10:13:32 ON 28 DEC 2007
L19             STR 64169-39-7
L20          12 SEA FAM FUL L19
L21           1 SEA ABB=ON  PLU=ON  L20 AND L2

     FILE 'CAPLUS' ENTERED AT 10:14:30 ON 28 DEC 2007
L22          52 SEA ABB=ON  PLU=ON  (L16 OR L20)(L)RACT+NT/RL
L23          48 SEA ABB=ON  PLU=ON  L22 AND L9
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L24          12 SEA ABB=ON  PLU=ON  L23 AND L11
L25          35 SEA ABB=ON  PLU=ON  L24 OR L13
L26        1762 SEA ABB=ON  PLU=ON  L6(L)(BAC OR DMA OR PAC OR PKT OR THU)/RL
                E SEROTONIN REUPTAKE INHIBITORS+ALL/CT
                E E2+ALL

     FILE 'HCAPLUS' ENTERED AT 10:17:59 ON 28 DEC 2007
L27        4439 SEA ABB=ON  PLU=ON  "5-HT REUPTAKE INHIBITORS"+PFT,NT/CT
L28         928 SEA ABB=ON  PLU=ON  L27 AND L26
L29        2478 SEA ABB=ON  PLU=ON  "5-HT REUPTAKE INHIBITORS"+PFT/CT
L30         533 SEA ABB=ON  PLU=ON  L29 AND L26
L*** DEL      0 S "5-HT REUPTAKE INHIBITORS"+PFT/CT(L)(BAC OR DMA OR PAC OR PKT
L31           3 SEA ABB=ON  PLU=ON  L30 AND L11
L32          37 SEA ABB=ON  PLU=ON  L31 OR L25
                E UTTARWAR S/AU

     FILE 'HCAPLUS' ENTERED AT 10:22:09 ON 28 DEC 2007

     FILE 'HCAPLUS, WPIX' ENTERED AT 10:22:12 ON 28 DEC 2007
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L33           2 SEA ABB=ON  PLU=ON  ("UTTARWAR S G"/AU OR "UTTARWAR SUNIL
                GOVINDRAO"/AU)
                E GAWLI B/AU
L34           2 SEA ABB=ON  PLU=ON  ("GAWLI B N"/AU OR "GAWLI BHAGWAN NARAYAN"/
                AU)
L35           2 SEA ABB=ON  PLU=ON  (L33 OR L34)
L36           1 DUP REM L35 (1 DUPLICATE REMOVED)
                      ANSWER '1' FROM FILE HCAPLUS

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L37           1 SEA L36
L38          37 SEA ABB=ON  PLU=ON  L32 OR L37

     FILE 'HCAPLUS' ENTERED AT 10:23:27 ON 28 DEC 2007
                D QUE L38
                D L38 IBIB ABS HITIND HITSTR TOT
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